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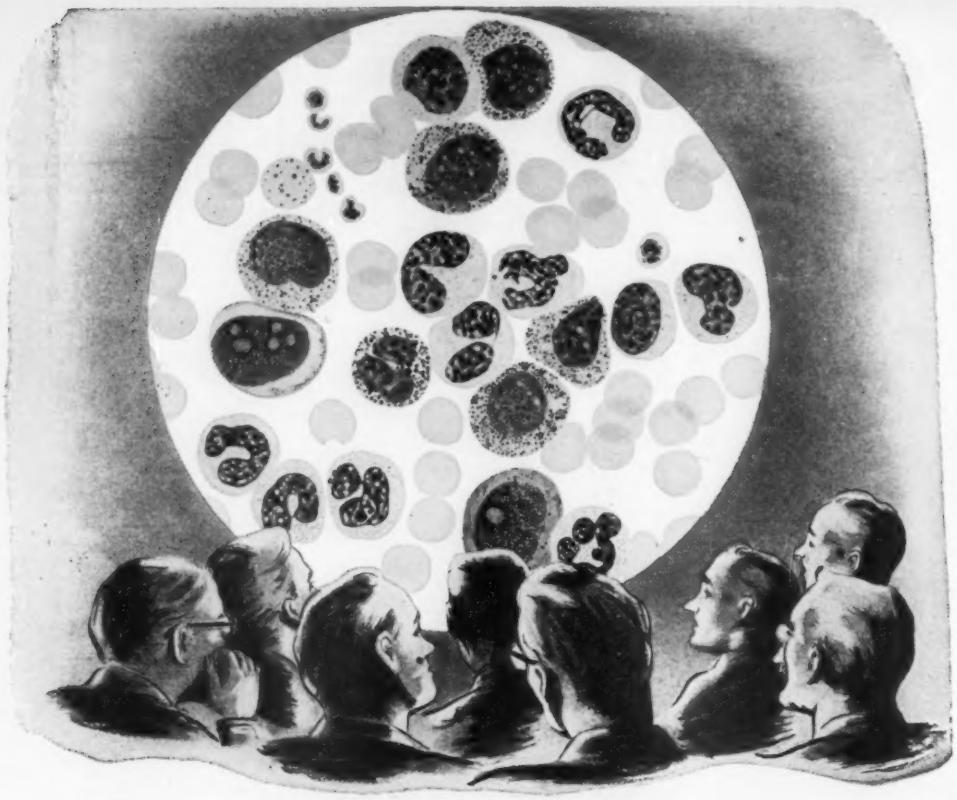

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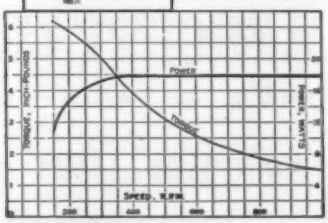

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Radiophysics in Australia

THE Radiophysics Laboratory in Sydney is a division of the Commonwealth Scientific and Industrial Research Organization, one of the main federal government agencies in Australia responsible for research and development in the fields of both primary and secondary industries. It had its origin in 1949 as a wartime radar research establishment but has since become a leading center for more fundamental research in radio and for the peacetime application of radar techniques to new fields. The laboratory is perhaps better known for its recent work in radio astronomy and radar meteorology, but it is also concerned with the development of new methods of navigation and of electronic computing devices of the digital type, the investigation of the upper atmosphere, and some research on the lower ionosphere.

Jansky's discovery (1932) of radio radiation from extra-terrestrial sources received new emphasis during World War II, when periods of high noise level on search radars as they scanned across the sun were found to have occurred when abnormally large sunspot groups were visible. Conclusive evidence that high-intensity radiation does originate in active areas on the sun, and that these are usually associated with sunspots, was obtained at the Radiophysics Laboratory in 1945. The novel techniques used—in which a single antenna mounted on a cliff overlooking the open sea, together with its mirror image, constitute an interferometer for observing radio sources as they rise above the horizon—have also been instrumental in discovering many of the known "radio stars," that in the constellation Taurus being the first to be identified with a known astronomical object (the Crab Nebula). The laboratory's current program covers almost the entire field of radio astronomy. Of particular interest in the solar field are the methods evolved for locating active areas on the sun, tracing their movement, and determining the polarization of the radiation from them; for observing the spectra of solar disturbances over the frequency range 40–240 mc/s in a fraction of a second; and for studying the distribution of radiation over the sun's disk. Early successes in the discovery of discrete sources are being followed up by measurements of their angular extent—which involves separations of some miles between the component antennae of the interferometer—and by observations of their frequency spectra. Evidence is being obtained that the discrete sources are largely, if not entirely, "radio nebulae." One exciting new line of work is a study of the 1420 mc/s line emitted by "cold" hydrogen, its profile and the Doppler shifts involved, its distribution in space, and the additional light these throw on the structure of our galaxy.

No less comprehensive is the laboratory's work on rain and cloud physics. Despite its early successes as a "rainmaker"—the first artificially produced rainstorm in which rain was conclusively shown to have reached the ground occurred near Sydney early in 1947—the laboratory has concentrated on obtaining a thorough understanding of the physical processes involved in the formation of clouds and rain. Theoretical work, backed by experimental verification, has been completed on the scattering of radio waves by meteorological particles; and, as a result of an active flying program in specially instrumented aircraft, the occurrence of substantial rainfall from nonfreezing clouds and the importance of coalescence as an alternative process in the growth of droplets to raindrop size have been amply documented. Artificial rainmaking is being investigated under controlled field conditions; the action of dry ice on supercooled clouds, for example, and the conditions under which its use is likely to be successful are now well understood.

In this brief outline many investigations in progress at the Radiophysics Laboratory have, of necessity, been omitted.

A. J. HIGGS

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Human Hemoglobin[1]

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ALTHOUGH DIFFERENCES IN THE PHYSICAL AND CHEMICAL PROPERTIES of human adult and fetal hemoglobins have been known for many years, the discovery of an electrophoretically abnormal hemoglobin in sickle cell disease provided the first positive evidence that adult human hemoglobin exists in more than one molecular form (*1, 2*). Two other species of adult human hemoglobin have now been described (*3, 4*), and an alkali-resistant hemoglobin component that has the properties of normal fetal hemoglobin has also been found in some anemic individuals (*5–11*). At least ten genetically distinct conditions that may be characterized by the hemoglobin composition of the erythrocytes have been observed, and it is of importance to the hemoglobin investigator to be able to recognize the presence of abnormal components in order to avoid the use of inhomogeneous preparations. To the geneticist and the hematologist the study of abnormal hemoglobins provides a method for differentiating inherited hematological abnormalities which other methods may fail to distinguish or even detect. One of the most significant conclusions based on these studies is that a molecular abnormality in a single protein may cause a sequence of events that characterizes a complex disease (*1*).

Fetal hemoglobin is produced in the human fetus and is the predominant form during prenatal life. At birth it comprises 55–98 per cent of the hemoglobin of infants (*8, 12, 13*). In the majority of healthy individuals this form of hemoglobin is no longer detectable after the first year of life, but in certain chronic anemias the production of fetal hemoglobin in varying amounts may continue indefinitely (Table 1).

Adult hemoglobin appears in the fetal blood early in prenatal life; in one 20-week fetus 6 per cent of the hemoglobin was of this form (*14*). It eventually replaces all the fetal hemoglobin in nonanemic individuals. *Normal adult hemoglobin* is the only form present in the great majority of adults. Three abnormal hemoglobins, all of which are rarer than normal adult or fetal hemoglobin and are associated with hematologic disorders, have been reported. From the biochemical and genetic evidence, which will be considered in this review, it will be evident that these are *abnormal adult hemoglobins* and not abnormal fetal hemoglobins that are being produced past fetal life.

TABLE 1

HEMOGLOBIN SPECIES PRESENT IN INDIVIDUALS WITH INHERITED AND ACQUIRED CONDITIONS

Condition	Species of hemoglobin present				
	a (normal adult)	*b* (sickle cell)	*c*	*d*	*f* (normal fetal)
Normal adult	+	–	–	–	–
" newborn	+	–	–	–	+
Sickle cell trait	+	+	–	–	–
" " anemia	–	+	–	–	+
Hemoglobin-*c* trait	+	–	+	–	–
Sickle cell–hemoglobin-*c* disease	–	+	+	–	±
Hemoglobin-*d* trait	+	–	–	+	–
Sickle cell–hemoglobin-*d* disease	–	+	–	+	+
Thalassemia minor	+	–	–	–	±
Thalassemia major	+	–	–	–	+
Sickle cell–thalassemia	+	+	–	–	+
Some acquired anemias	+	–	–	–	+

Sickle cell trait and sickle cell anemia are characterized by the presence of erythrocytes that are capable of undergoing changes in shape in response to changes in oxygen tension. When oxygenated, the cells are biconcave disks; when deoxygenated, they become sickle-shaped or multipointed. The erythrocytes in these two conditions differ in that a greater reduction in oxygen tension is required to induce complete sickling in sickle cell trait than in sickle cell anemia (*15*). The apparent relationship between oxygenation and sickling stimulated the initial studies in these laboratories of the hemoglobin in sickle cell disease (*1, 2*). The physical-chemical basis for the earlier observations was provided by the discovery that the hemoglobin in sickle cell anemia—a chronic, hemolytic anemia—consists mainly of a component having about three more net positive charges per molecule than normal adult hemoglobin in the pH range 5.7 to 8.0. In sickle cell trait, which is not associated with anemia, both this abnormal hemoglobin (named *sickle cell hemoglobin*) and normal adult hemoglobin were found in the same erythrocytes.

An early study of the inheritance of sickling resulted in the conclusion that a dominant gene is re-

[1] The abnormal hemoglobin studies at these laboratories were supported in part by grants from the National Institutes of Health of the U. S. Public Health Service. The guidance received from Ray D. Owen in the presentation of the genetics sections of this review is gratefully acknowledged.

[2] The author is assigned to the California Institute of Technology by the National Cancer Institute of the National Institutes of Health, U. S. Public Health Service.

[3] Contribution No. 1736.

sponsible for the transmission of this erythrocyte property (*16*), but no distinction was made between the modes of inheritance of sickle cell anemia and sickle cell trait. More recently it has been postulated that individuals with sickle cell trait are heterozygous in the gene for sickling, and those with sickle cell anemia are homozygous in this gene (*17, 18*). In accordance with the latter hypothesis, each parent of an individual with sickle cell anemia must carrry at least one gene for sickling; indeed, this situation occurs in the great majority of families in which the inheritance of this disease has been investigated (*19*). There are, however, some families in which only one of the parents of a child having hemolytic anemia associated with sickling cells has sickle cell trait. In each such case investigation has revealed a hematologic abnormality differing from sickle cell trait. In some of these families the diseased child has sickle cell hemoglobin and a second abnormal hemoglobin (*3*), which differs electrophoretically from both normal and sickle cell hemoglobins. The nonsickling parent has both normal adult hemoglobin and the second abnormal hemoglobin, and the sickling parent has the sickle cell trait mixture of normal adult and sickle cell hemoglobins. Normal children, sickle cell trait children, and children with the normal adult-second abnormal hemoglobin combination have also been observed in such matings (*3, 20*). In one family the nonsickling parent and two of the children had normal adult hemoglobin and a third abnormal hemoglobin (*4*) having the same electrophoretic mobility as sickle cell hemoglobin but a higher solubility. This hemoglobin and sickle cell hemoglobin were present in the diseased children. A fourth genetic type of sickle cell disease, in which the nonsickling parent has the thalassemia gene, is known (*21*). The erythrocytes of the anemic children have characteristics that reflect the influence of both the sickling and thalassemia genes. Both normal adult and sickle cell hemoglobins are present in the erythrocytes, but their relative amounts are abnormal (*11, 22*). In addition to the hemoglobin components described above, normal fetal hemoglobin may be present in each of the four anemias (*23*).

Nomenclature

The first abnormal hemoglobin has invariably been found in sickling erythrocytes and is appropriately named sickle cell hemoglobin, but the other abnormal forms are unnamed. Different symbolic representations for the human hemoglobins have been proposed (*9, 24*), but none of them includes all the known forms. The system I have proposed (*4*), now extended to include fetal hemoglobin, appears to be the most adaptable to future developments in the field, and will be used throughout this account. The two normal forms of human hemoglobin, normal adult and normal fetal, may be represented by their initials, *a* and *f*. The abnormal adult forms, sickle cell hemoglobin and the second and third abnormal hemoglobins, may be designated by the letters *b*, *c*, and *d*, respectively, in the chronological order of their discovery.

Sickle cell anemia, or sickle cell disease, is characterized by the presence of erythrocytes that become sickle-shaped when deprived of oxygen, and by symptoms and signs that are ascribable to a chronic hemolytic anemia and vascular occlusions. Some observers have felt that there are shades of variation in the severity of the anemia in this condition. Investigations in recent years, as cited above, have disclosed the basis for these observations; namely, there are four biochemically and genetically distinct conditions in which sickling erythrocytes and some or all of the classical symptoms of sickle cell anemia are present. In some cases there is little or no anemia. All these conditions may be grouped under the heading of sickle cell disease, but specific names should be given to each of the genetically distinct conditions. The name sickle cell anemia may properly be assigned to the type in which sickle cell hemoglobin is the only form of adult hemoglobin present, since this condition is always associated with anemia and undoubtedly includes the great majority of cases described in the literature as sickle cell anemia. A second form of sickle cell disease results from the simultaneous presence of the sickling and thalassemia traits, and may be termed sickle cell–thalassemia. The other two forms may be conveniently named sickle cell–hemoglobin-*c* disease and sickle cell–hemoglobin-*d* disease, after the two adult hemoglobins present in each of these conditions.

The asymptomatic condition in which sickle cell hemoglobin and normal adult hemoglobin are present has long been known as sickle cell trait, and the analogous conditions involving hemoglobin-*c* and -*d* may be called hemoglobin-*c* trait and hemoglobin-*d* trait, respectively. Although thalassemia major and its relatively mild counterpart, thalassemia minor (*25*), are not known to be characterized by the production of an abnormal form of hemoglobin, they are manifestations of an inherited abnormality in hemoglobin metabolism (*10*) and must be included in any discussion of abnormal hemoglobin syndromes.

Methods of Investigation

The use of hematologic methods is essential in selecting cases to be examined for hemoglobin abnormalities. The sickling test is a reliable criterion for the presence of sickle cell hemoglobin. Microcytemia, hypochromia, increased osmotic resistance of erythrocytes to hypotonic saline, and target cells are observed in the presence of the thalassemia gene (*21, 25*). A high incidence of target cells has been reported in the presence of hemoglobin-*c* (*24*). The determination of the survival time of transfused erythrocytes, although too laborious to be useful as a routine diagnostic procedure, has yielded much information on the behavior of abnormal erythrocytes in the circulation (*26–28*). The importance of familial hematologic studies in detecting the rare forms of sickle

cell disease is apparent from the earlier discussion.

The hemoglobin composition of the erythrocytes is established by physical and chemical methods. Electrophoretic analyses not only determine the species of hemoglobin but also the ratios in which they are present in an individual, and familial studies of these ratios have yielded significant genetic data (*20, 29*). Fetal hemoglobin can be identified most rapidly by its high resistance to denaturation (*11*) in aqueous alkaline solutions, by a maximum in its absorption spectrum at 2898 A (*13, 30*), and by paper chromatography (*31*). A rapid method for determining the solubility of amorphous ferrohemoglobin (*4*) has contributed to the identification of hemoglobin-*d*, which is indistinguishable electrophoretically from sickle cell hemoglobin. The procedure has been refined to increase its reproducibility and to permit a tentative differentiation among other abnormal hemoglobin syndromes (*11*). The refinement consists of the use of exactly 50 mg of hemoglobin instead of the large excess previously specified. Also, instead of a series of precipitating systems, only two, containing 8.00 ml and 9.20 ml of 2.80 *M* phosphate buffer, respectively, in a system of 10.00 ml total volume, are used; 100 mg of sodium dithionite, $Na_2S_2O_4$, is added to each system to ensure complete conversion to ferrohemoglobin. The precipitation and equilibration are carried out at 25° C.

Results

The electrophoretic properties that we have observed in the differentiation of the normal and abnormal human hemoglobins are summarized in Table 2. The data for hemoglobin-*c* and -*d* have been derived from analyses of mixtures, as neither form has been found free of either normal hemoglobin or sickle cell hemoglobin. In phosphate and cacodylate buffers of 0.1 ionic strength in the isoelectric region, normal adult, sickle cell, and hemoglobin-*c* have significantly different mobilities (*1–3*). Normal adult and normal fetal hemoglobin mobilities are nearly the same in these buffers, and mixtures of the two do not yield discrete boundaries on electrophoresis (*23*). In 0.01 *M* Na_2HPO_4, normal adult hemoglobin has a measurably higher mobility than fetal hemoglobin (*14*), and electrophoretic analysis in the Tiselius apparatus yields two-peak boundary diagrams. In this system the mobility of sickle cell hemoglobin is lower than that of fetal hemoglobin and that of hemoglobin-*c* is the lowest (*23*). These differences have been established by the examination of mixtures, since the poor buffering capacity of this system precludes precise determinations of absolute mobility. Sickle cell hemoglobin and hemoglobin-*d* have identical mobilities in all these buffers (*4, 23*), yet they are readily distinguished by ferrohemoglobin solubility determinations.

TABLE 2

Electrophoretic Properties of Human Hemoglobins

Name	Symbol	Isoelectric point*	Mobility at pH 6.5†	Relative mobility in .01 *M* Na_2HPO_4‡
Normal adult	*a*	6.87	2.4×10^{-5}	1
" fetal	*f*	—	—	2
Sickle-cell	*b*	7.09	2.9×10^{-5}	3
Second abnormal	*c*	—	3.2×10^{-5}	4
Third abnormal	*d*	7.09	2.9×10^{-5}	3

* Carbonmonoxyhemoglobin in potassium phosphate buffers of 0.1 ionic strength (*1*).

† Apparent mobilities of carbonmonoxyhemoglobin in cm^2 sec^{-1} $volt^{-1}$, calculated from ascending boundaries in cacodylate buffer of 0.1 ionic strength (*3, 32*).

‡ In order of decreasing mobility of the carbonmonoxyhemoglobins. The numbers have no quantitative significance.

TABLE 3

Solubility of Naturally Occurring Hemoglobin Mixtures Containing Sickle Cell Hemoglobin

Inherited condition	No. of individuals	Solubility* in g/liter
Sickle cell trait	15	1.28–2.17
" " anemia	7	0.14–0.44
Sickle cell–hemoglobin-*c* disease	5	1.13–1.23
" " " -*d* "	1	0.66
" " thalassemin	3	0.44–0.90

* As amorphous ferrohemoglobin at 25° C in aqueous system of 10.00 ml total volume, containing 8.00 ml 2.80 *M* phosphate buffer (*4*), 100 mg of $Na_2S_2O_4$, and 50 mg of hemoglobin.

The electrophoretic results described above have been observed in carbonmonoxyhemoglobin solutions. Ferrohemoglobin solutions have been examined in phosphate buffer, and the normal adult and sickle cell ferrohemoglobins exhibit a difference in isoelectric points similar to that between the corresponding carbonmonoxyhemoglobins (*1*).

The conditions of the modified amorphous ferrohemoglobin solubility method were chosen so that, in the absence of sickle cell hemoglobin, precipitation does not occur in the system containing 8.00 ml of phosphate buffer. Mixtures that go completely into solution in this system are then examined in the system that contains 9.20 ml of buffer. Tables 3 and 4 summarize the results of this method, which will be

TABLE 4

Solubility of Naturally Occurring Hemoglobin Mixtures Not Containing Sickle Cell Hemoglobin

Inherited condition	No. of cases	Solubility* in g/liter
Normal adult	7	1.29–1.65
" newborn	12	1.95–2.55
Hemoglobin-*c* trait	3	1.80–2.07
" -*d* "	1	1.34
Thalassemia minor	2	1.54
" major	1	2.30

* As amorphous ferrohemoglobin at 25° C in aqueous system of 10.00 ml total volume containing 9.20 ml of 2.80 *M* phosphate buffer (*4*), 100 mg of $Na_2S_2O_4$, and 50 mg of hemoglobin.

considered in detail in a separate paper. The procedure not only offers a rapid method for detecting the presence of sickle cell hemoglobin but also yields characteristic solubilities for the different mixtures. Among the specimens containing sickle cell hemoglobin, those from sickle cell trait have the highest solubility, and those from sickle cell anemia the lowest. The other three forms of sickle cell disease are characterized by intermediate amorphous ferrohemoglobin solubilities. In sickle cell anemia the solubility is increased by the presence of fetal hemoglobin (*4, 11*). The wide range in sickle cell trait solubilities reflects the variations present in the normal adult–sickle cell hemoglobin ratios (*32*). The narrow range of values in sickle cell–hemoglobin-*c* disease is consistent with the nearly constant percentage of sickle cell hemoglobin among individuals with this disease (*23*). Among the highly soluble mixtures, the hemoglobin-*d* trait mixture has nearly the same solubility as normal adult hemoglobin (*4*), and the hemoglobin-*c* trait and normal newborn mixtures have higher solubilities as amorphous ferrohemoglobin.

Fetal hemoglobin differs from all the adult hemoglobins in its electrophoretic, spectrophotometric, and alkali-resistant properties (*11, 12, 14*). In thalassemia major an alkali-resistant hemoglobin having solubility, crystal form, electrophoretic mobility, and ultraviolet absorption spectrum identical with those of normal fetal hemoglobin is present, together with normal adult hemoglobin (*8, 10*). The alkali-resistant component in the sickle cell diseases has been found to be identical electrophoretically, spectrophotometrically, and immunologically with normal fetal hemoglobin (*11, 23, 33*).

The denatured globins of sickle cell and normal adult hemoglobins have the same electrophoretic mobilities and patterns. The native globins, however, show the same difference in electrophoretic mobilities as the hemoglobins from which they were derived (*34*). This confirms a previous deduction (*1*) based on the identity of the hemes in the two hemoglobins, that it is in their protein portions that these molecules differ.

Discussion

Differentiation of adult and fetal hemoglobin. In a series of sickle cell anemia individuals, 2–25 per cent of the hemoglobin was found to have a high resistance to alkali denaturation (*9*). A similar component has been observed in two individuals with sickle cell–hemoglobin-*c* disease (*23*) and in two with sickle cell–hemoglobin-*d* disease (*4*). This component has the same electrophoretic, spectrophotometric, and alkali-resistant properties as the fetal hemoglobin of normal newborn infants and is not found in the parents of the diseased individuals. Apparently, the same component appears in some individuals with acquired anemias (*9*). In one anemic individual with bone marrow fibrosis and myeloid metaplasia of the spleen, about 10 per cent of the hemoglobin was found to be the alkali-resistant type, and the rest normal adult hemoglobin (*23*). The same alkali-resistant hemoglobin has therefore been observed in the presence of all the other hemoglobins in anemic individuals but not in nonanemic adults (Table 1). Sickle cell hemoglobin and hemoglobin-*c* and -*d* occur together with normal adult hemoglobin in nonanemic individuals; whenever any of these four is present in an individual, the same form has been found in one or both of his parents. The classification of hemoglobin-*b*, -*c*, and -*d* as abnormal adult hemoglobins and of the alkali-resistant form associated with anemia as normal fetal hemoglobin is based on the foregoing considerations.

The genetic control of the hemoglobin synthetic mechanism that results in formation of fetal hemoglobin is thus assumed to be distinct from that involved in the production of adult hemoglobin; it is the latter that is modified in the elaboration of hemoglobin-*b*, -*c*, and -*d*. The presence of fetal hemoglobin long after infancy may be regarded as evidence of a continuance or a reactivation of an essentially embryonic mechanism in compensation for an anemia resulting from a block in adult hemoglobin synthesis (*10*) or from a chronic hemolytic process.

Genetic relationships among the adult hemoglobins. The qualitative inheritance of the adult hemoglobins has already been reviewed. The study of the hemoglobin ratios in heterozygotes has shed light on the quantitative aspects of the genetic control of adult hemoglobins. The relative proportions of sickle cell and normal adult hemoglobins in sickle cell trait differ widely among individuals. Among the families in which this ratio has been studied, three modal values of the ratio are present. The data can be explained by postulating the existence of three iso-alleles for normal adult hemoglobin which are responsible for the net synthesis within an erythrocyte of the same molecule at different rates, and a fourth allele, which results in the net synthesis of sickle cell hemoglobin at a constant rate (*18*). In contrast to the varying ratio of normal adult to sickle cell hemoglobin among individuals with the sickle cell trait, the ratio of sickle cell hemoglobin to hemoglobin-*c* in sickle cell–hemoglobin-*c* disease has been found to be nearly unity in each of eight individuals from seven different families (*23*).

Although the genetic data at hand are so limited as to render a positive conclusion largely speculative at this point, they are consistent with the assumption that a single, multiple-allelic series affects the variety of adult hemoglobins known to exist. This series would include a group of three iso-alleles of the normal type, effecting the synthesis of normal adult hemoglobin at distinctive rates, as well as three aberrant alleles effecting, respectively, the synthesis of hemoglobin-*b*, -*c*, and -*d* (*20*).

Thalassemia is manifested by a decrease in the amount of hemoglobin per erythrocyte, and it has been postulated that the action of the thalassemia allele is to interfere with the synthesis of normal adult hemoglobin (*10*). In thalassemia minor the presence of one

thalassemia allele interferes sufficiently with hemoglobin synthesis to result in a low mean corpuscular hemoglobin but not a severe anemia; a small fraction of alkali-resistant hemoglobin may be present (*9*). Thalassemia major results from the presence of two alleles for thalassemia, one from each parent, both of whom must therefore carry the thalassemia allele. Homozygosity for this allele is associated with a drastic reduction of normal adult hemoglobin production, and a severe, chronic anemia results. Fetal hemoglobin may comprise from 40 to nearly 100 per cent of the total hemoglobin (*8–10*), but even this apparent compensatory effort is usually inadequate. The assumption of iso-alleles at the sickle-cell locus, which result in different rates of production of normal adult hemoglobin, may account for the variations that are observed in the severity of thalassemia major (*20*).

In sickle cell–thalassemia one gene for sickle cell hemoglobin and one for thalassemia are present. In the light of genetic evidence that the sickle cell hemoglobin and the thalassemia genes are not allelic with each other (*21*), sickle cell–thalassemia must commonly be associated with double heterozygosity, the normal allele at each locus being present, but heterozygous with an aberrant allele. Hemoglobin studies in sickle cell–thalassemia show that normal adult, normal fetal, and sickle cell hemoglobins are present (*23*). Unlike sickle cell trait, in which the fraction of sickle cell hemoglobin is less than half the total (*1*), sickle cell–thalassemia is characterized by a preponderance of sickle cell hemoglobin (*22*). The thalassemia allele would therefore appear to provide a more effective block to normal adult than to sickle cell hemoglobin synthesis.

The molecular disease hypothesis. When sickle cell hemoglobin was discovered, the available evidence was reviewed in support of a hypothesis that sickle cell anemia is caused by a single inherited molecular abnormality—namely, a difference in the surface configurations of sickle cell hemoglobin and normal adult hemoglobin, which enables the former to form more stable aggregates when deoxygenated (*1, 35*). It was postulated that this property was responsible for the intravascular sickling that has been observed in sickle cell anemia (*15*), and that the intravascular sickling rendered the erythrocytes more susceptible to destruction. The presence of a large fraction of normal adult hemoglobin in sickle cell trait erythrocytes was believed to interfere with the sickling process and to prevent its occurrence at the oxygen tension of venous blood. Subsequent studies on the solubility and tactoid formation of hemoglobin solutions are in accord with this hypothesis. Increase in the relative amount of sickle cell ferrohemoglobin results in increased tactoid formation in concentrated hemoglobin solutions (*36*) and decreased solubility in concentrated salt solutions (*4, 37*).

Survival studies of transfused erythrocytes support the view that increased hemolysis results from intravascular sickling. The survival of sickle cell anemia erythrocytes in the circulation approximates an exponential decrease with time, with a half-life of 29 days or less, indicating that the cells are destroyed in a random manner (*26, 27, 38*). In other words, the cells in sickle cell anemia have a similar susceptibility to destruction, regardless of their age (*39*). The administration of a high concentration of oxygen to sickle cell anemia patients has resulted in a significant decrease in the number of sickled forms in the circulation (*40*). Although determinations of total urobilinogen excretion have failed to indicate a decreased rate of hemolysis, the more direct and sensitive method of transfused cell-survival determinations has shown a marked decrease in the rate of cell destruction during oxygen administration (*27*). In contrast, the concentration of transfused sickle cell trait erythrocytes, which show little or no sickling in venous blood (*15*), decreases linearly with time, and the mean life of the cells is about 110–120 days, a survival behavior which is identical with that of normal cells, and which suggests that sickle cell trait cells are destroyed as a function of their age; i.e., the older cells are more susceptible to destruction.

The available data on the other forms of sickle cell disease suggest a significant correlation among ferrohemoglobin solubility, intravascular sickling, and severity of anemia. The average fraction of sickle cell hemoglobin in sickle cell–thalassemia has been observed to be somewhat lower than in sickle cell anemia but higher than in sickle cell trait (*11*). A hemolytic anemia is present (*21*), and in one individual whose hemoglobin was 70 per cent of the sickle cell form, intravascular sickling has been observed (*22*). In sickle cell–hemoglobin-*c* disease the fraction of sickle cell hemoglobin is about 50 per cent, compared to the 24–45 per cent found in sickle cell trait, and the ferrohemoglobin solubility is but slightly less. The hemolytic anemia associated with this condition is mild (*24*), and in one adult a normal value of blood hemoglobin concentration, 15 g/100 ml, has been observed (*41*). The hemoglobin composition in sickle cell–hemoglobin-*d* disease cannot be determined electrophoretically; it has been observed, however, that the ferrohemoglobin solubility lies between that of sickle cell trait and that of sickle cell anemia (*4*). Of the two individuals known to have sickle cell–hemoglobin-*d* disease, the one who is the more anemic has a lower ferrohemoglobin solubility. It is not known whether intravascular sickling occurs in sickle cell–hemoglobin-*c* disease and sickle cell–hemoglobin-*d* disease.

The high erythrocyte lipid content (*42*), the high incidence of target cells (*21, 24, 25*), increased osmotic resistance to hypotonic saline (*21, 25*), and the decreased survival times of nonsickling cells (*24, 28*), which have been observed in some of these conditions, deserve further investigation. There can be little doubt that the stroma changes reflected in these abnormalities are associated with the abnormal hemoglobin metabolism in the erythrocytes and result from the same genetic aberration that alters the metabolism.

Their role in causing the hemolytic anemia of the sickle cell diseases is probably a secondary one. The accumulated evidence is strongly in favor of the hypothesis that intravascular sickling, which occurs in the presence of a high proportion of sickle cell hemoglobin, is the major factor in the hemolytic anemia of sickle cell disease.

Conclusion

Our investigations to date have been concerned primarily with the detection of abnormal hemoglobins and the characterization of the mixtures in which they occur. It may be seen from Table 1 that normal adult hemoglobin is the only form that occurs free of other components. Further characterization will depend upon the isolation in a homogeneous state of each of the molecular species. Normal adult and sickle cell hemoglobins illustrate how two of the common criteria for homogeneity may be inadequate. These proteins have the same oxygen dissociation curve (*43*) and the same oxyhemoglobin crystal form and solubility (*44*). Thus, two molecular species of the same protein, which are present in the same sickle cell trait individual, have the same physiological activity and probably the same phase rule behavior, although they differ markedly in their electrophoretic mobilities and ferrohemoglobin solubilities. These observations re-emphasize the importance of the application of several independent methods to check the homogeneity of protein specimens used in fundamental studies, such as the determination of amino acid composition and sequence. Whenever inhomogeneity is found, the possible presence of an inherited abnormality must be considered.

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News and Notes

Informal Meeting of Representatives of Associations for the Advancement of Science

A meeting of representatives of Associations for the Advancement of Science was called by Unesco at Belfast on Sept. 5, 1952, during the meeting of the British Association, in pursuance of the first recommendation of the International Meeting of Associations for the Advancement of Science held at Unesco House in Paris Sept. 8–9, 1950; namely, "that authorized representatives of the various associations attending the meetings of other associations take advantage of the occasion to discuss matters of common interest." In attendance were members of the British Association: A. V. Hill (president), Richard Southwell, George Taylor, M. G. Bennett, D. N. Lowe, J. M. Robertson; British Council: W. R. McAlpine, Mary L. Logan; American Association: Detlev W. Bronk (president), Jeffries Wyman; Australian and New Zealand Association: J. E. Cummins; French Association: Jeane Verne; Indian Association: S. R. Sen Gupta, C. L. Parricha; Pakistan Association: S. D. Muzaffar, M. O. Ghani; Swiss Association: A. von Muralt (president). The Unesco representative was Gerald Wendt.

Invited but unable to attend were: American Association: Paul Klopsteg, chairman of the Commit-

tee on International Relations; Ceylon Association: S. Rajanayagam (president); Indian Association: Shanti Bhatnagar; Pakistan Association: Nazir Ahmad (president), Bashir Ahmad; South African Association: L. H. Wells.

On motion of A. V. Hill, the Unesco representative was designated chairman for the informal discussion. This being the first such meeting since the formal meeting of delegates of the science associations in Paris in 1950, the 16 recommendations made there were first reviewed, with reports on subsequent action and informal comment.

Recommendation 1 called for the establishment of a committee of representatives of all associations, as a coordinating and consultative body to advise Unesco with regard to desirable assistance to the associations. This committee was to function by correspondence until 1953, and Unesco was to consider the desirability of calling a meeting of the committee in that year. Only a few associations have specifically designated the officers with whom correspondence on international questions should be exchanged: the American Association appointed a Committee on International Relations comprising Paul Klopsteg, Karl Lark-Horovitz, and Kirtley F. Mather; the South African Association designated (in 1950) A. E. H. Bleksley; the Venezuelan Association indicated that the general secretary is responsible for foreign relations; and, for the Argentine Association, the president is responsible. As regards the 1953 meeting, the draft program and budget of Unesco for that year at present contain no provision for such a meeting.

Dr. Wendt pointed out that, unless other officers or committees were designated, he assumed that the secretary of each association is *ipso facto* the representative of his association on the international "coordinating or consultative body" and receives the quarterly letter on activities of the associations prepared by Dr. Wendt's office. He regretted, however, that few of the secretaries respond to these letters or report significant news to be incorporated in them, but this office does now receive the publications of all associations. Under these circumstances, the "international committee" has only a theoretical existence, and much remains to be done to develop an effective international body that can speak and act for the very important international aspects of science, especially with respect to the dissemination of scientific information, the improved teaching of science in schools, study of the worldwide consequences of scientific advances, the relations between scientific institutions and governments, and the mutual aid among the national associations. Most of the specialized sciences are organized into international unions, and these are related through the International Council of Scientific Unions, which is supported by a subvention of close to $250,000 a year from Unesco. But the larger problems of science and of its place in society are not now considered by anyone except Unesco itself and, there, receive less than 1 per cent of the budget. He regretted that so little progress had been made in the two years since the Paris meeting and that Unesco had not felt justified in calling a second formal meeting for 1953. He hoped that this and subsequent meetings of national associations would provide growing strength for an international movement which would develop a true international consciousness in the one great human activity that is inherently international.

Recommendation 2 urged that Unesco make funds available to assist new or weak associations. The Unesco Science Cooperation Offices, especially those for Latin America (Montevideo) and South Asia (New Delhi), have been actively assisting in the organization and expansion of new associations (Venezuela, Ecuador, Ceylon, Burma), and the East Asia Office at Manila is making earnest efforts to organize an Indo-Chinese association and to activate the Philippine Association, but no funds are available in the Unesco budget to assist such associations directly.

Recommendation 3 was to the effect that the associations extend reciprocal privileges to each other. This is now common but not universal. The large majority of the associations welcome the attendance of representatives of foreign associations at their annual meetings, although they cannot offer to pay expenses. In some cases, such guests are given the privileges of members of the inviting association (reduced registration fees, lodging arrangements) on a reciprocal basis. The Argentine, Brazilian, and Uruguayan associations have such agreements; the American Association offers these privileges to members of all associations. Furthermore, the American and British associations invite, as full guests, a limited number of representatives of fellow-associations. The American Association has also offered subscriptions to its magazines at membership rates to members of the British, French, and Italian associations and is awaiting the results of this step before extending it to others.

Recommendation 4 proposed that all associations should forward two copies of each of their publications to all other associations. This is now generally done. Dr. Gupta remarked that the cost of printing and mailing such copies to other associations, desirable as it is, is nevertheless a considerable item, as costs of printing mount progressively higher. Mr. Lowe remarked that this item of expense is so valuable that it should be among the very last to be cut from any budget. Dr. Wendt agreed to request the aid of the regional Unesco Science Cooperation Offices in assuring the distribution for the associations to whom the cost becomes burdensome.

Recommendation 5 asked that associations encourage their members who may be visiting other countries to attend association meetings there. This, too, is being done, but it is not often that members are visiting in foreign countries at the time of meetings, and there is no provision for financial support of such visits. Mr. Bennett commented that the interchange of visits and the presence of foreign scientists at meetings of the associations are, at the present stage of international relations, the most valuable means of contact and one that should be encouraged in all possible ways.

Recommendation 6 was to the effect that "the possibility be explored" of joint and regional meetings. One very successful experiment has been undertaken: the First Regional Meeting of Associations for the Advancement of Science held at Bangkok, November–December 1951. With the help of Unesco, a regional meeting for Latin America is now being considered for 1954.

Recommendation 7 urged the associations to set up national advisory press panels to which the press would turn for information, advice, and comment on scientific matters. This does not seem to have been implemented except by the South African Association, which established a press panel in December 1950 and began to issue a science newsletter for the local press.

Recommendation 8, that the associations inform Unesco of scientific films available in their country has unfortunately not borne fruit. But the International Scientific Film Association has now been organized, with offices at

164 Shaftesbury Ave., London, W. C. 2, and with member-organizations in Austria, Australia, Belgium, Brazil, Czechoslovakia, France, Great Britain, Italy, the Netherlands, Poland, South Africa, Switzerland, and Uruguay. This association publishes the quarterly *Science and Film*.

Recommendation 9 was to the effect that the various Associations for the Advancement of Science consult the Committee on Science and its Social Relations (CSSR), constituted by ICSU, on matters arising on the social implications of science.

Recommendation 10 was that the CSSR be invited to advise the various associations on its program of work and, further, that this body, wherever appropriate, be invited to consult with such associations on matters dealing with the social and international implications of science. Unesco is not informed that any major action has resulted.

Recommendation 11 suggested the inclusion of aspects of the social implications of science in the programs of the associations. This is a very general trend in most of the associations, but Unesco has received only scattered information on it.

Recommendation 12 was also on the interaction between science and society and called especially for contributions to the Unesco publication *Impact* and for the promotion of Unesco discussion themes. Meanwhile, the content and format of *Impact* have been radically changed in an effort to implement this recommendation, and the cooperation of the associations both in providing contributions and in assisting in the distribution of this quarterly is greatly to be desired. On the other hand, the organized promotion of the two Unesco discussion themes, "Food and People" and "Energy in the Service of Man," although markedly successful in some countries, failed completely in others. Except for one or two conspicuous exceptions, the contribution of the associations for the advancement of science was negligible.

Recommendation 13 was that associations encourage the formation in their countries of societies for visiting scientists of a type similar to those already existing in the United Kingdom, Belgium, and Canada. Unesco is not informed that anything has been done under this recommendation.

Recommendation 14 urged the publication and circulation at regular intervals of a card calendar of forthcoming events in the associations. The card calendar has not proved practicable, but the same purpose is accomplished now by the quarterly letters to the corresponding officers of each association from Unesco and the mailing of the DSIR "List of Forthcoming International Scientific and Technical Conferences."

Recommendation 15 requested Unesco to procure and make available high-level scientific articles to be used in the public press of other countries. Several qualified publications, particularly in the United States, have granted such permission to Unesco, but facilities have not been perfected for the distribution and release of such articles in other countries, and few requests for this service have been received.

Recommendation 16 was to the effect that Unesco study the possibility of approaching governments for the issuance of gratis study visas and for facilitating the temporary importation of scientific and educational materials by such visitors. Although no specific action on these precise points has been taken, Unesco has succeeded in obtaining governmental signatures to an agreement on the importation of educational, scientific, and cultural materials. An intergovernmental copyright conference, sponsored by Unesco, met in Geneva in September and discussed a new universal convention on copyright for later submission to governments.

Consideration of these 16 recommendations occupied the entire hour available for this meeting, so that no further items were considered. Mr. Lowe announced that the 115th annual meeting of the British Association will be held at Liverpool during the first week of September 1953 and that an even larger attendance of foreign guests was expected, so that a more fruitful discussion among foreign representatives could be anticipated at that time. There was no time to discuss the recommendations of the first regional meeting of Associations for the Advancement of Science held in Bangkok.

GERALD WENDT
Division of Teaching and Dissemination of Science
Natural Sciences Department, Unesco, Paris

Scientists in the News

Frank Aydelotte retired Jan. 1 as American secretary to the Rhodes Trustees, after 35 years of service. Dr. Aydelotte still heads the Association of American Rhodes Scholars, and will take an active part in organizing the American end of a Rhodes reunion in Oxford this spring. **Courtney Smith,** of Princeton University, has succeeded to the secretaryship.

Milo C. Bell, of Blaine, Wash., has been appointed a consulting engineer to assist in the further development of a federal fishery program for the Columbia River Basin. Mr. Bell has been chief technical adviser in the state of Washington's Department of Fisheries.

Three members of the Advisory Council of CSIRO, East Melbourne, Australia, have retired: **Harry Brown,** of the Radio Research Board, **Kerr Grant,** chairman of the South Australian State Committee, and **W. S. Kelly,** whose special knowledge relates to all phases of Australian primary industries.

V. D. Burgmann and **R. B. Coulson,** of CSIRO, East Melbourne, Australia, have been awarded the Bronze Medal of the British Institute of Navigation for the best paper published in the institute's journal during 1951.

Lester C. Dick has joined the Vick Products Division of Vick Chemical Company as assistant director of the pharmaceutical research laboratory at Bloomfield, N. J. Mr. Dick was formerly with G. S. Stoddard and Co.

P. A. M. Dirac, Lucasian professor of mathematics at the University of Cambridge, has been awarded the Planck Medal for 1952. The medal is given annually by the Association of German Physics Institutes for outstanding contributions to theoretical physics.

Four cash prizes have been awarded in the third competition sponsored by the Foster Welfare Foundation of Grand Rapids, Mich. **Charles H. Frantz** won

the award in the medical specialties class for his paper, "Orally-Given Mephenesin in Infantile Cerebral Palsy." The surgical specialties prize was presented to **Carl F. List,** for "Interhemispherical Subdural Suppuration." The general medicine award was shared by **Robert M. Eaton, J. Vincent Sherwood, Pearl L. Kendrick,** and **Grace Eldering,** for a cooperative paper, "Serum Protein Levels and Calculated Osmotic Pressures in Tuberculosis: Correlation of These Values with the Severity of the Disease." **Paul A. Van Pernis** received the prize in general surgery for his paper, "Variations of the Thoracic Duct," published in *Surgery.*

John L. Ham has been appointed project manager in the Metallurgical Department of the National Research Corporation, which will place him in charge of physical metallurgy.

Roger A. Harvey was appointed acting dean of the College of Medicine of the University of Illinois Jan. 1. In addition to his new position, he will continue as head of the Department of Radiology and as radiologist-in-chief of the university's research and educational hospitals.

J. T. Henderson, head of the electrical laboratory, Applied Physics Branch, National Research Council of Canada, was recently elected regional director for Canada of the Institute of Radio Engineers. A charter member of the Ottawa section of IRE, he served as vice-chairman of the section in 1949–50 and as chairman in 1950–51.

Harold L. James is visiting lecturer in geology at Northwestern University during the winter and spring quarters of the current academic year. He is on leave from the U. S. Geological Survey to teach and direct graduate research in petrology and ore deposits.

Meyer Kestnbaum, president of Hart, Schaffner & Marx, Chicago, has been elected chairman of the Committee for Economic Development, to succeed **Marion B. Folsom,** treasurer of Eastman Kodak Co., who has accepted appointment as Undersecretary of the Treasury in the new Administration.

Carl A. Lawrence has been appointed director of the Bureau of Laboratories of the Los Angeles County Health Department, succeeding **Raymond V. Stone,** who retired in January. Dr. Lawrence was formerly assistant professor of bacteriology at the University of Michigan Medical School and head of the Research and Control Divisions of the Winthrop-Stearns Chemical Company.

Lawrence P. Lessing has been appointed to the Board of Editors of *Scientific American.*

Jules Masserman, professor of nervous and mental diseases at Northwestern University and president of the Illinois Psychiatric Society, recently lectured to the Mexican Neuropsychiatric Society and Psychiatric Corps of the Mexican Army, and to the Cuban Society of Neuropsychiatry. Dr. Masserman and his associates have been granted $23,000 by the National Research Council for a continuation of their work on the biodynamics of experimental neurosis.

O. Kenton Neville, a pioneer scientist at Oak Ridge National Laboratories, has joined the Technical Division of Nuclear Instrument & Chemical Corporation, Chicago, as senior chemist.

Richard H. Nolte, a representative of the American University Field Staff, visited California Institute of Technology Jan. 12–21 to report on observations made in Egypt during the past two years. The AUFS was organized in 1951 by a group of American colleges and universities, under the auspices of the Institute of Current World Affairs, to send men into foreign areas, to study conditions and send regular reports to the participating sponsors.

Harold James Page has resigned as principal of the Imperial College of Tropical Agriculture in Trinidad to accept an appointment with the Food and Agriculture Organization of the United Nations.

C. W. Shilling, of the Medical Corps, U. S. Navy, has been awarded one of the Founders' Medals by the Association of Military Surgeons. **James M. Phalen,** editor of the *Military Surgeon,* and **Robert J. Benford,** coeditor of the *Armed Forces Medical Journal,* were similarly honored. The medals were authorized in 1941 to commemorate the 50th anniversary of the founding of the surgeon's group, and are awarded for outstanding contributions to military medicine.

Eric J. Simon has been appointed research associate in biochemistry at Cornell University Medical School. Dr. Simon will be engaged in research on muscular dystrophy.

Nicol H. Smith has been made director of the Franklin Institute Laboratories for Research and Development. Dr. Smith has been with the institute since 1932.

Two appointments on the RBD Committees on Guided Missiles and on Atomic Energy have been announced. **James C. Starks,** on leave from the Sandia Corporation, Albuquerque, N. M., has been named executive director of the Committee on Atomic Energy. **Allen E. Puckett,** head of the Aerodynamics Section of the Hughes Aircraft Company, will serve on the Committee on Guided Missiles.

Karl A. Stiles, professor of zoology at Michigan State College, has been named head of the Department of Zoology to succeed **Harrison R. Hunt,** who will retire July 1.

The Department of Commerce gold medal for exceptional service to the U. S. Coast and Geodetic Survey, and for outstanding leadership as its director, has been conferred upon **R. F. A. Studds.**

Norman Taylor, editor of *Taylor's Encyclopedia of Gardening,* left Jan. 18 for a three months' trip, visiting gardens in Egypt, Turkey, Greece, Italy, North Africa, and Spain.

Robert W. Webb has accepted the joint position of executive director of the American Geological Institute and executive secretary of the Division of Geology and Geography of the National Research Council. Dr. Webb is on leave of absence from the Department of Geology, Santa Barbara College.

Michael Woodruff, senior lecturer in surgery at the University of Aberdeen since 1948, has resigned to accept the Ralph Barnett professorship of surgery at the University of Otago, Dunedin, N. Z.

Education

Duke University is launching a nationwide forestry training program in cooperation with 22 other colleges and universities. Students will follow a three-year coordinated program in the basic arts and sciences at the participating schools and will then transfer to the Duke School of Forestry for two years of specialized training.

The **Oak Ridge School of Reactor Technology** will receive applications for advanced courses beginning in September up to *Mar. 1.* Industrial and other organizations that intend to sponsor students should file applications by *Feb. 1* if possible. For full information address the school at P. O. Box P, Oak Ridge, Tenn. Individuals should request application form A, and sponsors, application form B. F. C. Vonderlage is director of the school.

Stevens Institute of Technology will begin a series of ten lectures on corrosion Feb. 12, sponsored by the National Association of Corrosion Engineers. Robert S. MacCormack will be in charge of the series, and the lecturers will be T. P. May, F. L. LaQue, C. L. Bulow, H. W. Fritts, E. A. Tice, L. P. Sudrabin, A. R. Black, A. G. Gray, G. W. Oxley, and K. Tatot.

Vanderbilt University has established an annual lectureship in memory of Barney Brooks, late professor of surgery. The first lecture was given Jan. 21 by Evarts A. Graham, of Washington University, who spoke on "The Relation of Cigarettes to Bronchiogenic Carcinoma."

The annual Friend E. Clark Lectures at **West Virginia University** will be given by Herbert C. Brown, of Purdue University, on Feb. 23 and 24. He will discuss "Chemistry of Molecular Shapes" and "New Selective Reducing Agents."

At the **University of Wisconsin,** Asher Hobson, for 15 years chairman of the Department of Agricultural Economics, will retire Feb. 1 with the status of emeritus professor; Herbert R. Bird, of the Plant Industry Station, Beltsville, Md., will become professor of poultry husbandry; and George F. Hanson will become an instructor in the Department of Geology and Wisconsin state geologist, succeeding Ernest F. Bean, who recently retired from the latter post.

Grants and Fellowships

Bausch & Lomb Optical Co. has announced a new annual award in photogrammetry, open to any regular student, undergraduate or graduate, in a recognized college or university in the U. S. First prize is $100 and a three-year, paid-up membership in the American Society of Photogrammetry, and will be offered for papers of not more than 4000 words describing a new use of photogrammetry or of photogrammetric equipment, or describing an adaptation or improvement in the use of the science.

The **Institute of Gas Technology,** affiliated with Illinois Institute of Technology, has available 15 fellowships in mechanical and chemical engineering, and in gas technology. An accelerated program allows the master's degree to be earned in about 15 months in the first two subjects. Fellows may apply for extensions of their fellowships in order to work for the Ph.D.

Two **Lalor Foundation Fellowships,** with stipends of $1500 each, are available in the Department of Biological Sciences of the University of Delaware for research in the chemistry and physics of biological problems. For application blanks (which must be filed by *Mar. 1*) and full information, write to the dean of graduate studies.

Lehigh Portland Cement Company has established a new scholarship fund for students at Lehigh University with a gift of $20,000. The number of awards to be given each year will depend on the available income and the qualifications of the candidates. Applications for 1953–54 scholarships are now being received.

The **National Vitamin Foundation** has awarded new grants, totaling $61,500, to eight universities and two public health agencies. Recipients, who will work mainly on vitamin B_{12}, included Bacon F. Chow (Johns Hopkins); William J. Darby (Vanderbilt); Nevin S. Scrimshaw (Pan American Sanitary Bureau and Institute of Nutrition of Central America and Panama, Guatemala City); Richard W. Vilter (University of Cincinnati); H. D. Wallace, A. M. Pearson, and T. J. Cunha (University of Florida); A. E. Axelrod (Western Reserve); I. L. Chaikoff, Herbert M. Evans, and Marjorie M. Nelson (University of California, Berkeley); B. Connor Johnson (University of Illinois); Reginald F. Krause (West Virginia University); and Roberto Funaro (Nutrition Clinics Fund, New York, for continuation of studies in Italy).

The **Lowell M. Palmer Fund for Senior Fellowships** has been established at Cornell University Medical College with gifts from Carleton M. Palmer, former chairman of the board of E. R. Squibb & Sons, in memory of his father. Although the college will administer the fund, the recipients will not be limited to the Cornell staff. Five fellowships probably will be available during the first year.

Meetings and Elections

The **American Society of Photogrammetry** elected Alfred O. Quinn, of Aero Service Corporation, president at its annual meeting in Washington, D. C. Arthur C. Lundahl, of the U. S. Navy Photo Interpretation Center, and John I. Davidson, of the Tri-Metrogon Mapping Section, Alaskan Branch, U. S. Geological Survey, were elected first and second vice presidents.

Physiologists, biochemists, and pharmacologists from outside Canada and the U. S. who hope to attend the **International Physiological Congress** in Montreal, Aug. 31–Sept. 4, are asked to notify the secretaries of their national societies as soon as possible. In this way there will be time to arrange for special lectures and discussion meetings to be held in the Eastern U. S. or Canada near the time of the congress. Overseas scientists invited to take part in such functions will, in some cases at least, receive financial help that will appreciably reduce the cost of attending the congress itself. Scientists who live in countries where there are no national societies may write directly to the executive secretary, 19th International Physiological Congress, McGill University, Montreal. The position of the writer and his research interests should be given in each case. Booklets of general information have been mailed to the appropriate scientific societies; those not members of such societies, who wish to receive the information, should write to the executive secretary. Owing to an oversight, no form was included for the submission of films. Prospective members of the congress who wish to show films should write to the congress office before *May 1*, stating name of the author, title of film, running time, and whether 16mm or 35mm, silent or sound.

A **Symposium on Action of Ionizing Radiation on Biological Systems**, sponsored by the Institute of Polymer Research, Brooklyn Polytechnic Institute, will be held Feb. 7. The following speakers will participate in two panel discussions: Lloyd E. Brownell, Stephen L. Galvin, Samuel A. Goldblith, Bernard Manowitz, and John R. Matchett; W. Dexter Bellamy, Glenn C. Bond, Elmer L. Gaden, Jr., Nathan G. Kirsch, and Ernest C. Pollard.

Miscellaneous

The **American University**, in cooperation with the **National Bureau of Standards**, is sponsoring a weekly series of public lectures on "Theory of Games," beginning Feb. 10. For full information, call Woodley 6-6800 or address Walter F. Shenton, Department of Mathematics, American University, Washington 16, D. C.

The Annual Report (1951–52) of the **Indian Association for the Cultivation of Science** presents an account of research carried out in the departments of X-rays and Magnetism, Optics, and Physical Chemistry, as well as on projects sponsored by the Council of Scientific and Industrial Research of the Government of India. Crystal analysis, polymerization, synthesis, nuclear scattering, and x-ray studies of coal were among the subjects receiving special emphasis. During the year the association moved to new quarters in Jadavpur. P. Ray continues as honorary director, and J. C. Ghosh is president.

The **National Institutes of Health** new annual series of guest lectures began on Jan. 21. Severo Ochoa, of New York University of Medicine, spoke on "Tricarboxylic Acid Cycle: Enzymatic Mechanisms." The lectures will extend through May, with the following speakers: Douglas N. Buchanan, Bradford Hill, Harold G. Wolff, and C. N. H. Long. The series will be resumed in September.

New journals received: *Anales Instituto Nacional de Investigaciones Agronómicas* (Spanish). Vol. I, No. 2, Sept. 1952. Single copies, 25 pesetas. Ministerio de Agricultura, Madrid. . . . *Archivos Venezolanos de Patología Tropical y Parasitología Medica* (Spanish, with English summaries). Vol. II, No. 1, Jan. 1950. Instituto de Medicina Tropical, Universidad Central de Venezuela, Caracas. . . . *Bulletin d'Information* (French and Dutch). Quarterly; Vol. I, Nos. 1–2, June 1952. Institut National pour l'Etude Agronomique du Congo Belge, Brussels. . . . *The Gunma Journal of Medical Sciences* (this issue in English and German). Quarterly; Vol. I, No. 3, July 1952. Gunma University, School of Medicine, Mayebashi, Japan. . . . *The Journal of Clinical Nutrition.* Bimonthly; Vol. I, No. 1, Sept.–Oct. 1952. $6.00. Nutritional Press, 1631 Walnut St., Allentown, Pa. . . . *Journal of the Mechanics and Physics of Solids.* Quarterly; Vol. I, No. 1, Oct. 1952. £4. Pergamon Press Ltd., 2 Studio Pl., Kinnerton St., London S.W. 1. . . . *Library Trends.* Quarterly; $5.00. Each issue planned by a guest editor. Vol. I, No. 2, "Current Trends in Special Libraries," Herman H. Henkle, editor. University of Illinois Library School, Urbana. . . . *Materiae Vegetabiles* (English, French, German, Italian, or Spanish). Quarterly; Vol. I, No. 1, July 1952. 40 guilders. International Commission for Plant Raw Materials. Publishing office: W. Junk, 13, Van Stolkweg, The Hague. . . . *Memoirs of the Hyogo University of Agriculture.* Vol. I, No. 3, 1952. Biological Ser. No. 1, "Check List of the Fishes of Korea," by Tamezo Mori (English). Hyogo University of Agriculture, Sasayama, Japan. . . . *Proceedings of the Bihar Academy of Agricultural Sciences.* Three issues per year; Vol. I, No. 1, Jan. 1952. Rs. 10. Agricultural Research Institute, P.O. Sabour, Bihar, India. . . . *Reports of the Balneological Laboratory* (Japanese). No. 7, Aug. 1952. Okayama University, Misasa, Tottori, Japan. . . . *Revista de la Sociedad Cubana de Ciencias Físicas y Matemáticas.* Vol. II, No. 6, June 1952. $3.00. Universidad de la Habana, Edificio Poey, La Habana, Cuba. . . . *Student Medicine.* Semiannual; Vol. I, No. 1, Oct. 1952. Cayuga Press, Inc., Ithaca, N. Y.

Technical Papers

Oxidation of Disaccharide Alcohols by *Acetobacter suboxydans*[1]

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In connection with work on the constitution of planteose (*1*), we have been interested in various possibilities for the synthesis of oligosaccharides in which the reducing group is that of a ketose. Although the biological oxidation (*2*) of sugar alcohols by *Acetobacter* species has been used to prepare monosaccharide ketoses, we have been unable to find any record that this selective oxidation has ever been used to convert disaccharide sugar alcohols into the corresponding disaccharide ketoses.

We wish to report now some preliminary experiments on the behavior of disaccharide alcohols in *A. suboxydans* cultures. Typical 10-ml cultures contained 50 mg of yeast extract and 25 mg of sorbitol or mannitol (to ensure good growth of the organism) with or without 100 mg of the disaccharide alcohol. Samples were taken at intervals and analyzed for total reducing sugar and for the presence of reducing sugars (alkaline copper, heated, followed by phosphomolybdic acid) and ketoses (phloroglucinol-hydrochloric acid) on paper chromatograms.

Melibiitol (*3*), obtained by sodium borohydride reduction (*4*) of melibiose, was completely unaffected by the organism. Even after 46 days there was no evidence for the formation of any reducing sugar other than sorbose (from the added sorbitol). Since glycosides in general are not oxidized, the only position in melibiitol which would be configurationally suitable for oxidation would be position 5 of the sorbitol moiety. However, substitution of the galactosyl group on position 6 blocked oxidation.

Maltitol (*3*), similarly obtained from maltose and purified through the crystalline acetate, behaves in the same fashion. Here, substitution on position 4 of the sorbitol unit blocked oxidation at the otherwise available position 5.

Epimelibiitol (1-galactosyl mannitol) (*1*) was obtained in crude form by the acid-catalyzed condensation of galactose and mannitol. The preparation contained much mannitol, some mannitol anhydrides, and a mixture of the α and β galactosyl mannitols. On subjecting this mixture to the action of *A. suboxydans*, coincident with the formation of fructose there appeared a reducing disaccharide which had the same R_f value as planteobiose (*1*) and gave the characteristic color test for a ketose when sprayed with the phloroglucinol reagent. In this case, substitution of a glycosyl group at one end of the mannitol chain still leaves the other end unsubstituted and of the correct configuration for oxidation.

It is proposed, then, that this oxidation can be used for the preparation of keto disaccharides or higher oligosaccharides, provided that the corresponding sugar alcohols are available. We are now attempting to prepare workable quantities of planteobiose from purified epimelibiitol, and maltulose from turanose (through epimaltitol [*5*]).

[1] Journal Paper No. J-2124 of the Iowa Agricultural Experiment Station, Ames. Project 1116.

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Rh and ABO Blood Group Distributions in Japanese and Ethiopians

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Soon after the outbreak of hostilities in Korea a large-scale blood bank was activated in Tokyo. It supplied whole blood to medical units supporting United Nations forces in Korea and Japan. Most of its donor procurement and all its blood-processing operations centered in Tokyo.

Among the diverse racial and national groups volunteering as donors were numerous Japanese of the metropolitan area. Since these donors represented a realistic cross section of the indigenous population, it seemed appropriate to report some observations pertinent to them.

This paper records the Rh and ABO blood group distributions in 4541 native Japanese. It compares present findings with those described previously in Japan and in countries where persons of Japanese ancestry constitute a population minority. Data concerning frequencies in Ethiopian troops are also presented.

To ensure the accuracy of Rh[1] determinations, each blood was typed both by slide and by tube-centrifugation techniques. Fifty per cent concentrations of cells in their own serum were deposited on slides, mixed

[1] Refers to the Rh antigen most significant clinically, Rh_0 (D). Its presence in erythrocytes of any phenotype combination is demonstrated by agglutination with anti-Rh_0 serum. Lack of agglutination denotes its absence. Accordingly, persons with reactive cells are regarded as clinically Rh-positive; those with nonreactive cells are considered clinically Rh-negative.

TABLE 1

RH AND ABO FREQUENCIES IN JAPANESE AND ETHIOPIANS

Place	No. persons studied	Rh* (%)		Group (%)			
		Positive	Negative	O	A	B	AB
Japanese							
New York (1)	150	98.0	2.0	26.0	40.0	23.3	10.7
Denver† (2)	280	98.9	1.1	29.4	37.2	22.2	11.2
Canada (3)	606	98.9	1.1	—	—	—	—
Japan (Kumamoto Prefecture) (4)	459	98.5	1.5	—	—	—	—
Japan (Kumamoto Prefecture) (5)	1,011	98.7	1.3	—	—	—	—
Japan (nationwide) (6)	302,928	—	—	30.5	38.2	21.9	9.4
Japan‡	4,541	99.56	0.44	33.1	36.5	21.6	8.8
Ethiopians							
Ethiopia (6)	400	—	—	42.8	26.5	25.2	5.5
Korea‡	878	95.8	4.2	41.2	28.5	24.0	6.3

* Refers to reactions with anti-Rh_0 (anti-D) serum only.
† Group distributions based on 180 persons.
‡ Present study: Japanese in metropolitan Tokyo; Ethiopian troops with UN forces in Korea.

with 1 drop of anti-Rh_0 (anti-D) serum[2] and examined for agglutination within 5 min. All slide results were verified by tube tests in which cells from clotted blood were suspended to 2% concentration in one drop of anti-Rh_0 serum, centrifuged briefly, then read.

Blood groupings were carried out by tube-centrifugation procedures. Known anti-A and anti-B sera were used to classify the donor's cells. Conversely, known group A and B cells served to identify isoagglutinins in the donor's serum. Thus, the ABO group of each blood was established by its agglutinin as well as its agglutinogen content.

Table 1 compares data from representative surveys of Japanese and Ethiopians. It shows that of 4541 Japanese donors examined in the present investigation only 0.44% (20) were Rh-negative. This frequency is notably lower than the others listed. It is probable that the use of more effective diagnostic sera and techniques has minimized the occurrence of false negative reactions. Similarly, some Rh_0 antisera contained a mixture of D and D^u (Rh_0 intermediate) agglutinins in relatively high titer. The presence of this second antibody may have identified cells with D^u variant as Rh-positive, thus reducing the Rh-negative findings further.

In comparison with the others, the present survey indicates a moderately higher percentage of group O and slightly lower percentages of groups A, B, and AB Japanese. Since the earlier Ethiopian study did not include Rh data, only ABO group frequencies can be compared. These do not differ materially.

Table 2 shows that whereas the sexes in each group and the Rh-negatives in both sexes are almost equally distributed, the Rh-negative frequencies within each group vary substantially. To determine the statistical significance of these differences, the χ^2 test was applied only to the data for groups A and O, since groups B and AB do not have sufficient Rh-negatives for statistical test. Analysis reveals that the deviation in group A is not significant. However, the deviation in group O yields a χ^2 of 6.2 for 1 degree of freedom,

TABLE 2

RH-NEGATIVE DISTRIBUTION IN JAPANESE BY SEX AND BLOOD GROUP

Total persons studied	4541		
Rh-negative			20 (0.44)*
Male		3075	
Rh-negative			14 (0.46)
Female		1466	
Rh-negative			6 (0.41)
Group O	1501		
Rh-negative			13 (0.87)
Male		998 (32.5)†	
Rh-negative			9 (0.90)
Female		503 (34.3)‡	
Rh-negative			4 (0.80)
Group A	1659		
Rh-negative			6 (0.36)
Male		1145 (37.2)	
Rh-negative			4 (0.35)
Female		514 (35.1)	
Rh-negative			2 (0.39)
Group B	979		
Rh-negative			1 (0.10)
Male		663 (21.6)	
Rh-negative			1 (0.15)
Female		316 (21.6)	
Rh-negative			0 (0.00)
Group AB	402		
Rh-negative			0 (0.00)
Male		269 (8.7)	
Rh-negative			0 (0.00)
Female		133 (9.0)	
Rh-negative			0 (0.00)

* Figures in parentheses indicate percentages.
† Percentage of 3075 males; calculated similarly for groups A, B, and AB.
‡ Percentage of 1466 females; calculated similarly for groups A, B, and AB.

giving a probability of less than 0.02. It therefore seems unlikely that the observed difference is due to chance. Conceivably, a sample containing considerably

[2] Procured from American commercial sources, all antisera conforming to National Institutes of Health standards.

more Rh-negative individuals might alter present implications.

Although not recorded in the table, intergroup Rh-negative frequencies in Ethiopian troops showed no significant differences.

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Rooting Lemon Cuttings with Fruits Attached

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Detached lemon fruits are utilized in many research problems, of both a general and a specialized nature. A major drawback to their use has been the relatively short period during which they would remain turgid and more or less normal. The authors were concerned with prolonging the useful life of lemon fruits for studies of a physiological, biochemical, and entomological nature. A simple solution to the problem seemed to be the production of roots on stems attached to the fruits. Such a technique should not only result in maintaining healthy turgid fruits for long periods under the usual conditions of high humidity but should permit studies involving low relative humidity.

This paper presents the results obtained in an experiment to determine the rooting response of lemon cuttings with fruits attached.

Two hundred and forty-nine medium-sized lemons ranging in color from yellow to light-green were clipped from several Eureka lemon trees on Feb. 7. Stems on the fruits varied from 1 to 2 in. in length, and approximately half of them had one or two leaves attached. The fruits were segregated into three color groups of yellow, silver, and light-green. The silver category is a packing-house designation for yellow fruit which still retains a slight amount of green color, usually at the ends. Each color group was subdivided into cuttings with and without leaves. These groups were further divided into groups to be treated with a rooting preparation (0.2% naphthalenacetic acid on talc, ANA) or left untreated. The cuttings were placed in a rooting bed with sand as a rooting medium and were usually sprinkled two or three times daily during the rooting period.

Fig. 1. Rooted lemon cutting without leaf but with light-green lemon attached.

A count of rooted cuttings and roots was made on Mar. 6, 4 weeks after the start of the experiment. The results are presented in Table 1 and Fig. 1. Cuttings with light-green lemons attached rooted most readily, whereas those with yellow lemons rooted least readily. The presence of leaf tissue appeared to be unnecessary in the cuttings with light-green and silver lemons but necessary for root formation in the cuttings with yellow lemons. Naphthalenacetic acid increased the percentage of rooted cuttings in all comparisons.

Leafy lemon cuttings have been reported to root better than leafless ones (*1*), even when treated with a growth regulator such as indolacetic acid (*2*). Cooper (*3*) suggested that the role of indolacetic acid was to mobilize, at the base of the cutting, rhizocaline, a root-forming factor produced in the leaves. On the

TABLE 1

Rooting Response of Lemon Cuttings

	Light-Green				Silver				Yellow			
	Leaves		No leaves		Leaves		No leaves		Leaves		No leaves	
	No ANA	ANA	No ANA	ANA	No ANA	ANA	No ANA	ANA	No ANA	ANA	No ANA	ANA
No. cuttings	38	37	31	26	21	22	13	12	13	15	10	11
Percentage rooted	31	59	52	81	10	68	15	67	8	67	10	18
Roots per rooted cutting	1.8	3.8	3.3	3.0	1.5	4.4	1.5	2.4	1.0	3.9	5.0	7.5

other hand, Gregory and van Overbeek (*4*), van Overbeek and Gregory (*5*), and van Overbeek, Gordon, and Gregory (*6*) showed that the leaves of red-flowered hibiscus cuttings could be replaced by a treatment with sucrose and nitrogen, insofar as the number of roots formed was concerned.

In the present study it was found that leaves were not essential for the rooting of leafless cuttings when light-green or silver-colored lemons were attached. It appears, therefore, that immature lemon fruits can supply the same factors as are ordinarily supplied by the leaves. Sugars (*7, 8*) and nitrogen (*9*) are present in both green and yellow lemons. Whether these factors become less available for mobilization to the base of the cutting as the fruit matures or whether other factors for rooting are concerned requires further investigation.

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The Stimulation *in Vitro* of Phospholipid Synthesis in Thyroid Tissue by Thyrotrophic Hormone

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The tissue slice technique has proved a most useful tool in investigations of the metabolism of the thyroid gland. Studies in Chaikoff's laboratories (*1, 2*) showed the ability of surviving thyroid slices to synthesize diiodotyrosine and thyroxine from inorganic iodine. With the same technique, the inhibition of thyroxine and diiodotyrosine synthesis by large amounts of iodide (*3*) and the effects of goitrogens (*4*) on the organic binding of iodine were demonstrated.

The present results appeared during the course of a study (*5*) of the possible correlation between phosphorus and iodine metabolism in a similar system of thyroid slices. A striking stimulation of the rate of incorporation of phosphorus into the phospholipids of thyroid tissue was found when thyroid slices were incubated in a medium containing radioactive orthophosphate in the presence of the thyroid-stimulating hormone (thyrotrophin, TSH) of the anterior pituitary gland. No such effect was observed in either the trichloracetic acid soluble or insoluble fractions.

Beef thyroid[1] was used. The procedure of slicing and incubation was as previously described (*1*). A total of 300 mg of tissue slices was incubated in 3.00 ml of Krebs-Ringer bicarbonate medium at pH 7.4, 37° C, under 95% oxygen and 5% CO_2 for a 3-hr period. Approximately 1 μc P^{32} as orthophosphate[2] was used in each beaker. Thyrotrophin,[3] dissolved in the buffered medium, was used in the concentrations noted in Table 1. The analytical procedure used will appear elsewhere (*5*).

The data of Table 1 demonstrate the marked stimulation of thyrotrophin (TSH) on the incorporation of radioactive orthophosphate into the lipid fraction of surviving thyroid slices. An amount of TSH as low as 0.3 J.S.[4] units produced phospholipid synthesis of the order of 181% that of controls. The maximum stimulation observed was 254% of the control, using 6–8 units of TSH (1 mg) in the bath. These findings suggest that this system may well be at least as sensitive as that of Borell and Holmgren (*6*) in the assay of pituitary thyrotrophin.

Dialysis of the protein hormone against 50 volumes of distilled water did not decrease its activity in promoting the incorporation of P^{32} into the lipid fraction. This would seem to rule out any effect from small molecule contaminants such as choline. A further test of this possibility showed that 1 mg choline/3 ml medium had no effect.

The specificity of this action is shown by a study with liver and kidney slices using 3 times as much TSH as was used with thyroid tissue. There was no evidence of any increase in P^{32} incorporation in the

[1] Grateful acknowledgment is made to Don Sherman, of the Alpha Beta Meat Packing Company, Wintersburg, Calif., who made available the beef thyroids used in this study.

[2] The radiophosphorus used in this investigation was supplied by Oak Ridge National Laboratory on authorization from the Isotopes Division, U. S. Atomic Energy Commission.

[3] Grateful acknowledgment is made to Wayne Donaldson, of Parke-Davis & Co., for the thyrotrophin used in this study.

[4] Junkmann-Schoeller.

TABLE 1

Effect of Thyrotrophin (TSH)* on Uptake of Radiophosphate by Phospholipids of Beef Thyroid Slices

Expt. No.	S-3-125	S-5-23	S-3-125†	S-3-119	S-3-115	S-3-115	S-3-115
Mg TSH in medium	0.01	0.038	0.1	1.0	5	10	15
% increase P^{32} over control	105 ± 11	181 ± 16‡	180 ± 11	254 ± 12	217 ± 9.9	208 ± 9.6	210 ± 8.4

* In all studies Parke-Davis TSH Rx 099802, estimated to contain 6–8 u/mg, was used.
† Thyrotrophin treated by dialysis against 50 vol distilled water for 48 hr.
‡ σ for $n = 4$; in all other studies $n = 2$.

liver and kidney lipids, whereas in the same study the thyroid lipids were 184% of the control. The USP Reference standard for TSH gave similar results.

A more complete report and discussion of the mechanism of the thyrotrophic hormone effect on phosphorus metabolism of the thyroid will be presented elsewhere.

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A "Fly Factor" in Attractant Studies

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The importance of species odors in integrating the group behavior of social insects and in the mating of insects generally has long been recognized. That similar factors may play a role in the formation of other insect aggregations is less widely known, although some evidence for such mechanisms has been reported, as, for example, for caterpillars of *Pieris brassicae* by Fabre (*1*) and for the cockroach by Ledoux (*2*).

During field tests of the possible usefulness of attractant baits as a supplement to other methods of housefly control, it became apparent that the flies themselves must produce or bear some substance attractive to others of the species (*Musca domestica* L.). In these experiments, 15 g aliquots of a stock prepared by boiling 100 g white corn meal in 100 ml water were used extensively as nonattractant, nonrepellent control baits and as a vehicle for the various substances that were to be tested as attractants. The baits were exposed in the vicinity of a dairy barn which was supporting an estimated population of about 50,000 flies, and it was observed regularly that fly counts on the control baits increased with increasing exposure time (Table 1).

TABLE 1

Fly Counts on Mush Control Baits

Exposure time (min)	Date of test										Total flies
	9/21	9/21	9/21	9/25	9/25	9/27	9/27	10/5	10/5	10/17	
5	0	0	0	1	1	0	3	2	3	0	10
10	1	0	0	1	4	4	3	4	7	0	24
15	2	1	3	7	5	2	2	8	13	0	43
20	1	2	4	4	8	4	2	7	1	4	37
25	1	9	10	4	22	2	5	10	10	6	79
30	7	4	2	7	17	3	5	15	11	8	79
35	4	11	0	5	28	7	9	7	21	7	99
40	12	6	5	10	27	11	7	10	33	18	139
45	9	14	9	6	26	18	4	11	31	23	151
50	17	15	10	10	38	16	7	8	29	16	166

The possibility that this phenomenon was associated merely with the drying of the mush or its exposure to air was eliminated by placing in the test position paired mush baits, one of which was protected from contact with flies by a screen cover. After 30 min, the screen was removed and periodic counts were made of the flies visiting each dish. Results are shown in Table 2.

TABLE 2

Attraction of Flies to Screened and Unscreened Baits

Time after removal of screen (min)	No. pairs tested	Total no. flies on baits	
		Previously unscreened	Previously screened
5	4	24	2
10	4	39	7
15	3	28	6
20	2	18	8
25	2	25	13

The further possibility that the position of the dish or memory on the part of the flies could be concerned was ruled out by experiments of the following type. Three baits in Petri dishes were placed in a row in the test position. The two outer dishes, one of which was screened, contained identical mush baits; the center dish held an attractant (Diamalt). After the dishes had been in place for 20 min, a picture was taken which showed numerous flies on the Diamalt, a moderate number on the uncovered mush, and none of course on the mush that was screened. Immediately thereafter, the screen was removed, the positions of the mush baits exchanged, and all flies driven off. A second photograph, 4 min later, recorded essentially the same distribution of insects as the first; i.e., the mush that had been screened initially was still free of

flies, whereas the other baits were being visited as before. The dishes were now shifted so that the Diamalt occupied the right-hand position and the originally screened mush bait the center. The flies were again chased away. Once again, as seen in a picture taken 6 min later, the flies chose the previously visited mush bait in preference to the one that had been covered. They also found their way back to the Diamalt bait in large numbers. The dishes were then returned to their original positions and all flies chased away. Five min later a final photograph was made, in which it was once more apparent that the mush previously visited by the flies was more attractive than the sample that originally was screened. However, one could see also that the number of flies on the formerly screened sample had begun to increase.

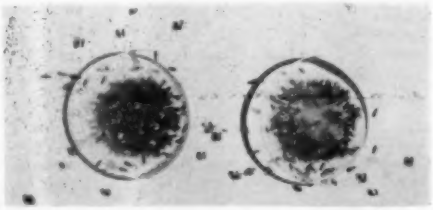

FIG. 1. Effect of previous feeding on attractiveness of proteose peptone to flies. Left-hand dish exposed 20 min, right-hand dish 2 min.

Variants of this test, in which portions of each bait were covered for a time with adhesive tape, and in which the dishes were rotated through various angles or exchanged in position through various sequences, were repeated several times with similar results, proving conclusively that it is visitation by flies and not some other factor that renders either mush or Diamalt baits more attractive. This same effect was observed also with baits initially more attractive than the foregoing materials. In Fig. 1, for example, are shown two dishes, each containing a very attractive mixture of proteose peptone and water. The dish at the left had been subjected to heavy feeding by flies for about 20 min, whereas that at the right had been exposed for only about 2 min.

It is logical to conclude from such data that flies that visit a bait contribute to it some substance which enhances its attractiveness to the species. The nature of this substance is unknown, although we have found that a material attractive to flies and soluble in 95% ethanol, but much less soluble in acetone or ether, can be extracted from the bodies of these insects. Further efforts to isolate and identify this substance, and to determine whether it is identical with that contributed to baits by flies which visit them, are planned.

Meanwhile, the observations outlined above are of obvious significance for the design and interpretation of field experiments on fly attractants. Valid conclusions in regard to the attractiveness of test materials will be possible only when experiments are so arranged as to permit a distinction between attraction exerted by the test compounds and that derived from previous contact with the insects.

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Distribution of Allergic and "Blocking" Activity in Human Serum Proteins Fractionated by Electrophoresis Convection[1, 2]

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The purpose of this investigation was to determine the distribution of allergic, or reaginic, antibodies in human serum proteins. Electrophoresis convection was chosen as the means of fractionation of these skin-sensitizing antibodies not only because of its gentle nature but also because sufficient volumes of fraction are involved to permit complete immunologic and electrophoretic characterization—objectives precluded by the small yields of conventional electrophoresis. Whereas the latter procedure led Newell *et al.* (*1*), as well as Sherman and Seebohm (*2*), to conclude provisionally that reagins for pollen resided in γ-globulin, the factors responsible for "cold" allergy appeared more disseminated. Cooke and collaborators (*3*) later concluded that the γ-globulin activity of individuals allergic to animal dander, pollen, or mold spores was about 10 times *lower* than the corresponding dilution titer of the original serum. Campbell and associates (*4*) were the first to apply the method of electrophoresis convection to the problem. They found that activity was closely associated with the α- and β-globulins in one serum, whereas it appeared to be distributed among all the globulins in another.

In the present investigation, electrophoresis convection has been extended to 7 stages, rather than 3, and the more reliable "passive transfer" procedure of neutralization with allergen *in vitro* has been added to the technique of serum dilution employed exclusively by earlier workers. Sufficient material was also available to do titrations in three normal test subjects, as well as to observe the fractions for stability during a 4½-month period. Furthermore, electrophoretic analysis and chemical assays for protein content were done on each preparation.

[1] This investigation was supported in part by the Office of Naval Research, the U. S. Public Health Service, the National Institute of Arthritis and Metabolic Diseases, the Damon Runyon Fund, and the American Cancer Society.

[2] Presented in part before the second International Congress of Biochemistry in Paris, July 21–27, 1952.

[3] The authors wish gratefully to acknowledge the valued suggestions of John G. Kirkwood.

Fractionation. The details of construction and operation of the electrophoresis-convection apparatus, as well as its application to the separation of serum proteins, have been described by Kirkwood *et al.* (*5–7*). A woman highly allergic to all preparations of commercial insulin served as the source of the 70 ml of serum needed for fractionation. At the conclusion of each run, the contents of the upper reservoir were passed through a bacterial, Seitz filter and were set aside at 4° C for future study under the label Top 1 or 2 or 3, etc. "Bottom" solution remaining in the cell was then diluted for the next run. Whereas the first 6 stages were carried out in phosphate buffer of 0.1 ionic strength during 48–51 hr at field strengths ranging from 1.5 to 2.5 v/cm, acetate buffer of the same ionic strength was employed for the 7th run of 73 hr. The pH levels chosen for successive runs were 7.5, 7.0, 6.5, 6.0, 6.0, 5.3, and 5.2. After the last stage, bottom fraction was separated into a globulin and an albumin portion by adding one volume of saturated ammonium sulfate at pH 7. The globulin fraction was further purified by reprecipitation, then labeled BG-7 to distinguish it from the albumin, BA-7.

Electrophoretic analysis was done on a 1% solution of each fraction, pervaporation being necessary in the case of the top and albumin preparations. Barbital buffer at pH 8.6, ionic strength 0.1, and a field strength of about 7 v/cm were employed for the 2-hr runs in the apparatus of Perkin and Elmer, voltage being measured with a potentiometer. Mobilities were calculated (*8*), and the relative area of each component was determined by the use of a planimeter on a projected tracing of the descending pattern. It was then possible to estimate the protein concentration for individual components, since the protein content of each fraction had been established and the contribution of its several components to the total area had been measured.

TABLE 1

ESTIMATED PROTEIN CONTENT OF VARIOUS ELECTROPHORETIC COMPONENTS*
(mg/ml)

Fraction	Assayed protein content of fraction	Albumin	α_1-globulin	α_2-globulin	β-globulin	γ-globulin
Whole serum	70.0	35.0		4.2	19.6	11.2
Top 1	3.1	.06			.1†	2.9
Top 2	2.7	.08			.1	2.5
Top 3	0.8	Trace			< .1	.7
Top 4	0.9	"			.2	.6
Top 5	0.3	"			.1	.2
Top 6	4.2	.4		1.0	2.1	.7
Top 7	8.9	1.9	2.6	1.6	2.9	
Bottom 7	43.0	34.4	4.3	3.0	1.3†	
BA-7	43.0	37.8	(———	5.2	———)	
BG-7	5.6		2.8	2.8		

* Area of component in per cent was multiplied by assay figure for protein content of fraction.
† Estimate unreliable, as β-globulin comprised only 3% of area.

TABLE 2

DISTRIBUTION OF SKIN-SENSITIZING POWER IN HUMAN SERUM PROTEINS AFTER FRACTIONATION BY ELECTROPHORESIS CONVECTION
(As judged by *in vitro* neutralization with allergen [insulin])

Fraction	Total protein (mg/ml)	Insulin required to neutralize fraction		Insulin required to neutralize globulins (u/mg protein)	
		u/ml	u/mg total protein	Total globulins	β-globulin
Whole serum	70.0	35.0	0.5	1.0	1.8
Top 1	3.1	0.25	0.08	.08	2.7*
Top 2	2.7	0.25	0.09	.01	1.6
Top 3	0.8†				
Top 4	0.9†				
Top 5	0.3†				
Top 6	4.2	5.0	1.2	1.3	2.4
Top 7	8.9	7.5	0.85	1.1	2.7
Bottom 7	43.0	1.0	0.02	0.12	0.8*
BA-7	43.0	0.25	0.006	0.05	*
BG-7	5.6	0.5	0.09	0.09	

* Electrophoretic area too small for reliable estimate.
† Sensitizing power almost negligible.

Activity tests. Each fraction was given a preliminary test for sensitizing power, 0.1 ml of undiluted material being injected intracutaneously into a normal volunteer. In 24 hr each site received 0.025 ml of Squibb crystalline insulin containing 4 u hormonal activity/ml. Allergic potency was judged by the size of the wheal-and-flare which promptly developed. Immunologically active materials were subsequently examined in serial twofold dilutions, as well as admixed in undiluted state with an equal volume of insulin in doubling concentrations. One-tenth ml from each tube was then injected into the skin of one of three normal subjects for test with insulin next day, so as to reveal the greatest dilution in which each fraction could transfer sensitivity, as well as the minimal amount of insulin required to neutralize its sensitizing power (*9, 10*). Although the relative potencies of the various fractions were roughly confirmed in two other recipients, it will suffice to present the results of one subject, E.M.M. Only those obtained during the first few weeks of study will be given, since the fractions (but not the original serum) showed decided loss of potency during the 4½ months of observation.

Tops 1–4 were found to contain fractions of the γ-globulin of the original serum, with a mobility spectrum ranging from -1.31×10^{-5} to -1.91×10^{-5}. Tops 1, 2, and 3 consisted almost exclusively of γ-globulins (95–90%). Tops 5, 6, and 7 were the richest in β-globulins, containing 39, 50, and 32%, respec-

tively. Whereas BG-7 was comprised entirely of α_1- and α_2-globulins, fraction BA-7 was 88% albumin, according to planimeter measurements. Table 1 lists the protein content of the several components of each fraction, as calculated from its chemical and electrophoretic analyses, and subsequent tables express activity in terms of potency per mg of component protein.

The conclusion was drawn that activity is associated almost exclusively with β-globulin, this deduction being based on the following analysis. First, albumin and the α- and γ-globulins were excluded from consideration as major contributors of activity, inasmuch as an upper limit of very low order could be put on each of them. Fraction BA-7, for example, contained 88% of albumin but required only 0.25 u insulin/ml for its desensitization (Table 2). This amounts to only 0.006 u insulin/mg albumin. Similarly, Tops 1 and 2 were comprised of 95 and 91% γ-globulin, and carried this same low neutralization requirement. If the activity were attributed exclusively to γ-globulin, its neutralizing power amounted to only 0.08 u/mg, or less.

The α_1- and α_2-globulins were judged by fraction BG-7, which was comprised solely of these two proteins and possessed an activity of only 0.09 u insulin/mg, a finding discouraging to assumption that α-globulins might play an important role. If all the sensitizing power of the whole serum had been referable to its α-globulin component, this would have had to carry a requirement amounting to 8.35 u insulin/mg α-protein. The discrepancy between this and the above observation for BG-7 is inconsistent with the proposition that the α-globulins carry significant activity.

In contrast with the foregoing, high activity was exhibited by Tops 6 and 7, both of which contained large proportions of β-globulin. Making the most liberal allowance for activity of the α-globulins in these fractions, based on BG-7, the neutralizing power

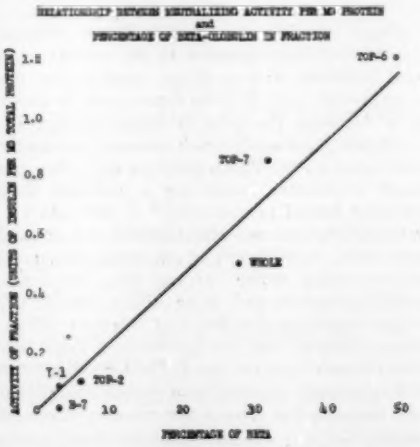

FIG. 1.

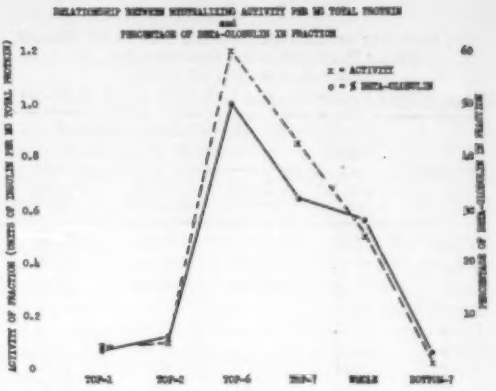

FIG. 2.

of β-globulin/mg was calculated to be 2.4 u insulin for Top 6 and 2.7 u for Top 7. This is over 20 times the maximal potency that can be attributed to either the γ- or the α-globulins.

Further evidence for the hypothesis that activity resides principally in β-globulin is furnished by the observation that the activity per mg determined for Top 1 is roughly 2.7, for Top 2 approximately 1.6, and for whole serum, 1.8—values which can be considered constant within the limits of the assay method employed. (Bottom-7 and BA-7 are not included in this discussion because their β-globulin areas were too small for reliable estimates.) On the other hand, the assumption that reagins are uniformly distributed among all the globulins is untenable in view of the computed activities per mg of total globulin, since they are by no means constant, ranging from 0.01 to 1.3 (Table 2).

In Fig. 1, the activity per mg of total protein is plotted as a function of the percentage of β-globulin in the several fractions. It will be observed that, within the limits of experimental error, the neutralizing power is proportional to the β-content, which is consistent with the hypothesis that activity resides in the β-globulin and that it amounts to approximately 2 u/mg. In Fig. 2 the percentage of β-globulin and the activity per mg of total protein are shown to be precisely correlated. The conclusion to be drawn from the foregoing evidence is that β-globulin possesses a neutralizing activity at least 20 times greater than that of any other protein in the serum. This is confirmed by the serum-dilution results for the various fractions, the order of potency closely following that of the neutralization end points (Tables 2 and 3). Fractions with small dilution ratios possessed low concentrations of β-globulin, as will be noted in Table 1. Tops 1 and 2, for example, contained only about 0.1 mg/ml. The right-hand column of Table 3 shows that the maximal dilutability of a solution containing 1 mg β/ml was approximately 1:10, indicating that the minimal strength for borderline sensitization was

TABLE 3

DISTRIBUTION OF SKIN-SENSITIZING POWER IN HUMAN SERUM PROTEINS AFTER FRACTIONATION BY ELECTROPHORESIS CONVECTION

(As judged by sensitization tests with serial dilutions)

Fraction	Dilutability of original fraction	Dilutability of solution containing 1 mg/ml of		
		Total protein	Total globulin	β-globulin
Whole	256	3.7	7.4	13.2
Top 1	2	0.65	0.66	21.5*
Top 2	2	0.75	0.76	12.5
Top 3	< 1			
Top 4	< 1			
Top 5	< 1			
Top 6	24	5.7	6.3	11.4
Top 7	32	3.6	4.6	11.2
Bottom 7	4	0.09	0.47	3.0*
BA-7	1	0.02	0.19	*
BG-7	2	0.35	0.35	

* Electrophoretic area too small for reliable estimate.

roughly 0.1 mg β/ml, as determined from Tops 6 and 7, which transferred markedly in our subject when employed in their original concentrations. The feeble sensitizing qualities of all other fractions were, therefore, consistent with the concept of β-activity.

It will be remarked that Tops 3, 4, and 5 could not be used in the analysis of β-activity (Tables 2 and 3), since they transferred only questionably in E.M.M. From Table 1 it will be noted that the β-globulin concentration of Tops 3 and 5 approximated 0.1 mg/ml, the figure mentioned above as the borderline requirement. Top 4, with its content of 0.2 mg, should have produced detectable sensitization. Although it failed to do so in E.M.M., it transferred slightly in another recipient, resembling Tops 1 and 2 in potency, as might have been expected from its rather low β-content.

Since the writing of this paper, another serum containing reagins (for ragweed pollen) has been similarly fractionated and studied by the dilution technique. Activity appeared to be distributed through the γ- and β-globulins. The maximal volume in which 1 mg of total protein would still transfer sensitivity ranged from about 1 ml for Top 1, which consisted predominantly of γ-globulin, to approximately 4 ml for Top 7, the β-rich fraction. These results suggest that allergic activity is concentrated in β-globulin. However, it was not restricted to this protein as in the instance of our insulin-reaginic serum.

The pollen-reaginic serum also contained thermostable, or so-called blocking, antibody. Its presence in the fractions was judged by the amount of pollen antigen each could neutralize, heated samples being mixed with graded strengths of pollen extract for subsequent test in sensitized normal skin. Neutralizing activity was found in fractions rich in γ-globulin. Top 1 (consisting 91% of a slow γ-globulin having a mean mobility of -1×10^{-5}) possessed a neutralizing power of about 10 phosphotungstic-acid-precipitable N u pollen/mg total protein. Top 5 (containing 70% of fast γ-globulin, with a mean mobility of -2×10^{-5}) carried an inhibiting activity of over 30 u/mg in two test subjects. Antibody content appeared to be minimal in Tops 2 and 3, which were composed largely of γ-globulin of intermediate mobility. The remaining fractions, comprised almost exclusively of β-globulins, α-globulins, or albumin, showed negligible neutralizing power. We therefore conclude that the thermostable antibody is concentrated in the γ-globulins, with a bimodal distribution. The latter might be attributable to the existence of more than one antibody for the multiple antigens known to be present in pollen.

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Effect of Halogens on the Production of Condensation Nuclei by a Heated Platinum Wire

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Experiments performed in this laboratory show that the presence of small traces of gaseous halogens or halogen-containing compounds in the atmosphere causes a very large increase in the rate at which a heated platinum wire produces condensation nuclei. The apparatus used in these experiments is shown in Fig. 1. Air from the room is drawn through a long filter of fine glass wool, which removes practically all condensation nuclei. This nuclei-free air is then passed through a chamber containing a platinum filament electrically heated to about 500° C and into an apparatus which measures the concentration of condensation nuclei. In this work an automatic condensation-nuclei-measuring device (*1*) was used, but less complicated equipment, such as an Aitken counter (*2*) or a simple expansion chamber, is satisfactory. When the platinum filament was first turned on, a large concentration of nuclei was produced. The formation of these nuclei apparently resulted from surface contamination of the filament, for after a few minutes of operation

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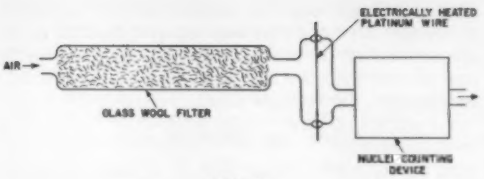

FIG. 1.

the filament ceased producing any nuclei, and the air entering the measuring device became nuclei-free.

It was observed that when small amounts of gaseous halogen or halogen-containing substances such as Cl_2, I_2, Br_2, and CCl_4 were present in the air being drawn through the filter the heated platinum filament produced large numbers of nuclei. The sensitivity of the apparatus to CCl_4 was found to approach that of the commercial halogen leak detector which operates on the positive ion emission of a heated platinum filament.

A possible explanation for this phenomenon is as follows. At 500° C the vapor pressure of platinum is so low that an insufficient concentration of atoms is introduced into the air to condense and form condensation nuclei. The halogen or halogen-containing gases in the air, which pass freely through the glass wool filter, react with the hot platinum surface. The resulting compounds, although relatively nonvolatile at room temperature, have a higher vapor pressure than the platinum and at 500° C are vaporized in sufficient concentration to condense upon mixing with air at room temperature to form large numbers of nuclei.

It is reasonable to suppose that other systems can be devised in which small concentrations of certain gaseous materials will result in the production of large numbers of nuclei from certain nonvolatile substances maintained at an elevated temperature.

The fact that nuclei having masses of the order of 10^{-17} g are readily detectable in concentrations as low as 10/ml suggests that very sensitive analytical techniques based on nuclei detection are feasible.

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Analysis of Dose-Response in Relation to Mechanism of Pulmonary Tumor Induction in Mice

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It is almost universally assumed that the transformation of cells to malignancy involves some change in the cell. The nature of this change remains one of the basic questions in cancer research. Berenblum and Shubik (*1*) have postulated a two-phase process, the initiative phase and the promoting phase, a concept that has been supported by others. Blum (*2*) has suggested that in the induction of skin tumors by ultraviolet irradiation there is progressive acceleration of growth by successive doses. This suggests that there may be successive changes in the cell.

Much consideration has been given to the somatic mutation theory of carcinogenesis proposed by Von Hansemann and later by Boveri, and recently vigorously supported by Strong (*3*) and others. Although the number of changes might not necessarily be limited to one, the present concept of this theory would tend to locate the change or changes in the nucleus, presumably as gene changes.

Interest in the somatic mutation hypothesis recently has been strengthened by the general search for a positive correlation between mutagenic and carcinogenic capacities of chemicals. An over-all positive correlation has not been observed, but isolated experiments testing related compounds under standardized conditions have presented positive correlations that in themselves suggest that possibly the change to malignancy is basically genic. Tests in this laboratory (*4, 5*) on the induction of pulmonary tumors in strain A mice with mustard compounds have shown that both the nitrogen mustard, methyl-bis (2-chloroethyl) amine hydrochloride, and sulfur mustard, bis (2-chloroethyl) sulfide, which Auerbach (*6*) and others have shown to be strong mutagens, were also potent carcinogens, whereas mustard oil, ethyl iso-thiocyanate, which was found to be a very weak mutagen, did not significantly increase the number of lung tumors.

In an analysis of the number of papillomas observed in mice painted repeatedly with Benzpyrene, Charles and Luce-Clausen (*7*) demonstrated a linear relationship when the square root of the number of papillomas was plotted against time, an expression of dose. This suggested the necessary occurrence of two separate events, or mutations, in the cell for the induction of a papilloma, the requirement if a recessive mutation were involved.

From our experience with pulmonary tumors in mice, it seemed desirable to analyze the pulmonary tumor response to graded doses of a carcinogen to ascertain whether here also would be found a parabolic curve indicating more than one change, or a straight line, as could be expected if only one change were necessary for a cell to give rise to a tumor. Certain outstanding advantages are offered by this type of tumor: (1) the many nodules appearing on the surface of the lungs afford a quantitative measure of response; and (2) a single dose of the carcinogen, even of very small amount, gives a measurable response. Thus, repeated doses such as were encountered in the studies of papillomas and Blum's radiation studies could be avoided.

[1] With the technical assistance of W. D. Levillain.

Five groups of strain A mice approximately 2 months old were injected intravenously, respectively, with .1, .2, .3, .4, and .5 mg 1:2:5:6-dibenzanthracene in colloidal dispersion in .5 ml distilled water/mouse.[2] A sixth group was injected with .5 ml distilled water as controls. The sexes were approximately equally divided in all groups, and the mice were individually identified. They were kept in plastic cages, 8 mice to the cage, fed Derwood pellets, and given an unlimited supply of tap water. Six months after the injection all animals were killed, their fresh lungs were examined with the aid of the dissecting microscope, and the number of tumors appearing on the surface of the lungs of each animal was recorded.

The average number of tumors for each dosage group is listed in Table 1. Sexes are combined, since no sex difference was observed.

TABLE 1

PULMONARY TUMORS IN STRAIN A MICE INJECTED INTRAVENOUSLY WITH 1:2:5:6-DIBENZANTHRACENE

Dose (mg)	No. animals	Av no. nodules	SE of av no.
0.	55	.29	.033
.1	51	8.08	.542
.2	50	18.25	1.225
.3	44	30.02	1.663
.4	50	38.64	1.923
.5	46	53.37	2.166

Subject to certain limitations, the tumor-dose relationship is linear. The limitations require that one postulate the operation of two conflicting endogenous factors. The first of these is a tumor-increasing factor, the genetic susceptibility of the strain. Some animals that have received no dibenzanthracene at all will develop tumors. This means that a dose of zero is effectively zero plus this small factor, designated as G, and other doses are not .1 mg, .2 mg, etc., but rather $.1+G$, $.2+G$, etc. Operating in the other direction, there appears to be a factor reducing the effective amount of the carcinogen. Perhaps a small amount is lost in the circulation prior to reaching the lungs, or in some other way a small amount is eliminated or made ineffective. This represents a sort of "threshold" dose. Calling this factor R, one finally would have as the effective dose, the reported dose $+(G-R)$.

If one fits a least-squares straight line to the data, excluding the response at the reported zero dose, one gets for the constants of the equation

y = average number of tumors $= a + bx$
$a = -2.86$
$b = 108.35$

This implies that at zero dose there should be expected an average of -2.86 tumors per animal. However, we are not really interested in fitting $y = a + bx$, but rather in fitting $y = a' + b[x + (G-R)]$. If we can do this we can make an estimate of the combined factor $(G-R) = k$. At the zero reported dose the average number of tumors per animal from the experimental data was .29. This is a'. Then we can write, setting $x = 0$, for the zero dose:

$$-2.86 = .29 + 108.35\ (0 + k).$$

Then $k = (G-R) = -.0293$, and the equation is: average number of tumors $= .29 + 108.35$ (dose $- .0293$).

This equation fits the data very well, as shown in Fig. 1. A test of accuracy of fit (χ^2) gives a nonsignificant deviation from linearity; that is, there is no statistical evidence that the linear hypothesis is inadequate to explain the results.

Postulating a "threshold" dose implies that for doses less than .03 mg dibenzanthracene, there should be no greater response than at a zero dose. Of course one cannot expect this sort of sharp break to occur. The value .03 (that is, .0293) is subject to error, and, in addition, individual animals could be expected to have individual abilities to "dispose" of some small amount of the carcinogen. What might be expected is that the portion of the curve between 0 and .1 would have a smooth form, concave upward, rather than a sharp breaking form (Fig. 1).

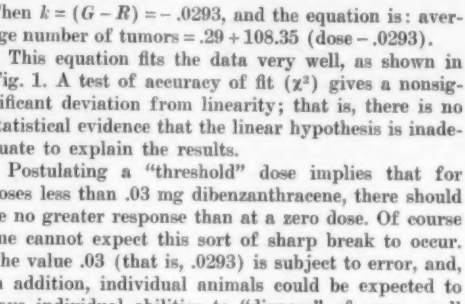

FIG. 1.

An attempt was made to fit the data to the two-action hypothesis set forth by Charles and Luce-Clausen (7), which implies that the square root of the number of tumors is proportional to the dose. It was barely possible to fit a least squares straight line that was not outside the $2\times$ standard error of mean limits. χ^2 is 5.405, which with two degrees of freedom, gives a probability of so large a deviation from the fitted line (due to chance alone) of between .10 and .05. The two-action hypothesis leads to a positive constant to be added to the dose rather than the negative constant found for the single-action hypothesis. This

[2] This dispersion was prepared by Joanne Hollcroft.

constant was higher than could be accounted for on the basis of the incidence of spontaneous tumors in this strain. The hypothesis implies an average of more than 3 tumors at the zero dose, whereas the observed average was .29. This increased response is even more difficult to explain than the decreased response shown for the single-action hypothesis. The two-action hypothesis implies that the curve is concave upward, which would give a rapidly increasing number of tumors at the larger doses. Instead, at the higher doses the curve probably would be found to flatten out. Since there is also a time element involved if the actual response curve is sigmoid, observing the tumors earlier might give an upward curve, whereas later observations might give a downward curve. This requires further investigation.

Data on pulmonary tumors induced in mice with methylcholanthrene by Shimkin and McClelland (*8*) were examined to see if the linear relationship between the number of nodules and the dose was also present in their experiment. Such a linear relationship could not be established, there being significant departure from linearity when the χ^2 test was used. However, there were not as many animals per group in their experiment as in the groups reported herein, and the technique used in counting was not the same for the two experiments. In their experiment the nodules were counted in lungs that previously had been fixed in Tellyesniczky's fluid, and apparently the counting was done without the aid of the dissecting microscope. Their data did not fit a parabolic curve such as reported by Charles and Luce-Clausen either.

It was possible, however, to estimate the "net disposal" constant (k) for Shimkin and McClelland's data such as was estimated from our own experiment. Their data were in three series, with observations made after 8, 13, and 18 weeks. For these series, k was .047 mg, .040 mg, and .047 mg methylcholanthrene, respectively. These constants are more nearly alike than would have been expected from the variance of k which is implied by the mathematics.

Although the data of Shimkin and McClelland do not support, they do not oppose our own data, which with the analysis thereof would fit the postulate that the induction of pulmonary tumors in the mouse is the result of a single change in the cell. If this were a genic change it would be assumed to be a dominant mutation.

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Ascorbic Acid and the Oxidation of Tyrosine

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Many lines of evidence have suggested that ascorbic acid is involved in the biological oxidation of tyrosine. Studies with rat liver homogenate preparations (*1*) and acetone powder extracts (*2*) have indicated that the effect of ascorbic acid in the conversion of tyrosine to acetoacetic acid is primarily upon the first oxidative step of this metabolic pathway, the oxidation of *p*-hydroxyphenylpyruvic acid. Recently it has been proposed that ascorbic acid is a cofactor for the enzyme catalyzing this oxidative step (*3*). In the present communication, evidence will be presented that ascorbic acid may have a less specific role and can be replaced by a number of structurally unrelated compounds that are susceptible to oxido-reduction.

In experiments with extracts of liver acetone powder of rat, rabbit, and dog, it has been reported that tyrosine, *p*-hydroxyphenylpyruvic acid, 2,5-dihydroxyphenylpyruvic acid, and homogentisic acid oxidized enzymatically to acetoacetic acid (*2, 4*). The addition of ascorbic acid to this preparation increases the oxidation of tyrosine or *p*-hydroxyphenylpyruvic acid but has no effect upon the oxidation of 2,5-dihydroxyphenylpyruvic acid and homogentisic acid (*2*). The effect of ascorbic acid on the oxidation of *p*-hydroxyphenylpyruvic acid can be studied by using either *p*-hydroxyphenylpyruvic acid as the substrate or by using tyrosine with α-ketoglutarate to generate *p*-hydroxyphenylpyruvic acid via the tyrosine transaminase system present in the extract. The effect of ascorbic acid was established by measuring the rate of disappearance of substrate and by following the reaction manometrically in the Warburg apparatus. When 10 μM of L-tyrosine was used as the substrate with the liver extract preparation, the addition of ascorbic acid increased the oxidation of tyrosine only when α-ketoglutarate was also present, as shown in Fig. 1. A concentration of 0.001 *M* (4 μM) ascorbic acid was found to be sufficient to produce a maximal stimulatory effect upon the oxidation. Further increase in the concentration of ascorbic acid did not increase the initial rate of oxygen uptake, nor did it alter the products of the reaction. Suboptimal concentrations of ascorbic acid resulted in less tyrosine being converted to acetoacetic acid.

The preparation of the acetone powder removes part of the ascorbic acid orginally present in the tissue. The residual amount remaining in the crude powder extract is sufficient, however, to maintain appreciable oxidative activity. Dialysis of the crude

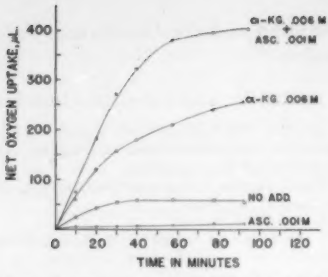

FIG. 1. The stimulation of L-tyrosine oxidation by ascorbic acid (ASC) in the presence of α-ketoglutarate (*α-KG*). Flask contents: 2.0 ml rabbit liver powder extract; 1.0 ml pyrophosphate buffer; 0.3 ml α-ketoglutarate (20 μM) or 0.3 ml of H_2O. The side arms contained 10 μM L-tyrosine in 0.5 ml phosphate buffer (buffer alone was used in the control flasks), and 0.2 ml ascorbic acid (4.0 μM). Total volume, 4.0 ml. Both α-ketoglutarate and ascorbic acid were omitted in the no-addition flasks (*No ADD.*).

powder extract greatly reduces the ability to oxidize *p*-hydroxyphenylpyruvic acid, but this activity is nearly completely restored by the addition of ascorbic acid to the dialyzed extract system.

Considerably less than stoichiometric amounts of ascorbic acid are needed for the oxidation of tyrosine. Titration with 2,6-dichlorophenolindophenol at the end of the incubation period has shown that nearly half the added ascorbic acid remains in the reduced form. Since the titration values are the same for the control flasks and the ones in which tyrosine was oxidized, it appears that no net consumption of ascorbic acid is required for the oxidation of tyrosine.

Although these results are in agreement with the theory that ascorbic acid acts as a cofactor for the enzyme system catalyzing the oxidation of *p*-hydroxyphenylpyruvic acid, the data presented below suggest that ascorbic acid may act in a less specific manner.

Knox (*1*) observed in experiments with the rat liver homogenate preparation, that D-isoascorbic acid also increases the oxidation of tyrosine. We have tested several compounds using the acetone powder extract preparation and have found that D-isoascorbic acid, D-ascorbic acid, and hydroquinone are just as effective as L-ascorbic acid on a molar basis. Homogentisic acid, *p*-aminophenol, *p*-phenylenediamine, and 2,6-dichlorophenolindophenol also increase tyrosine oxidation but are less effective than ascorbic acid. On the other hand, catechol, resorcinol, 3,4-dihydroxybenzoic acid, 3,4-dihydroxyphenylalanine, dihydroxymaleic acid, cysteine, and glutathione are unable to replace ascorbic acid or to supplement a suboptimal concentration of ascorbic acid. The oxidized forms of ascorbic acid or hydroquinone (dehydroascorbic acid or quinone) are nearly as effective as the reduced forms. This would be expected if these compounds undergo cyclic oxidation and reduction during the oxidation of tyrosine.

The observation that several compounds are able to stimulate the oxidation of *p*-hydroxyphenylpyruvic acid suggests that the requirement is one for a compound having the proper oxidation-reduction potential. Whether these compounds found to be active in place of ascorbic acid function by protecting the small amount of ascorbic acid present in the powder extract or completely replace ascorbic acid in this system cannot be determined without further purification of the enzyme system involved.

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Manuscript received July 8, 1952.

Comments and Communications

Zoological Nomenclature

NOTICE is hereby given that, as from June 29, 1953, the International Commission on Zoological Nomenclature will start to vote on the following cases involving the possible use of its plenary powers for the purposes specified against each entry. Full particulars of these cases were published on Dec. 29, 1952, in the *Bulletin of Zoological Nomenclature* in Double-Part 4/5 of Vol. 9. (1) *Astacus Fabricius*, 1775 (Class Crustacea, Order Decapoda), validation of (correction of an error in Opinion 104); (2) *Favus* Lanchester, 1900 (Cl. Crustacea, Ord. Decapoda), validation of (correction of an error in Opinion 73); (3) *flavipes* Olivier, 1795, *Dytiscus* (Cl. Insecta, Ord. Coleoptera), validation of, by the suppression of *flavipes* Fabricius, 1792, *Dytiscus*.

Comments on the above cases should be sent as soon as possible to the undersigned.

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Scientific Conferences and Papers

IT SEEMS worth while at this time, when so many conferences on such a variety of subjects are scheduled, to review the fundamental purposes of a scientific conference and the methods of best achieving these ends.

The principal objective of a scientific conference

should be, of course, the advancement of the science. We firmly believe that this aim can best be implemented by providing sufficient time for adequate discussion of the controversial points and, subsequently, by publishing the papers *and* discussions as a unit. The feasibility and utility of allowing ample time for discussion and of reporting the entire proceedings in one volume depend on the type of conference. The type best suited to these arrangements is a meeting of specialists primarily interested in a particular field and mentally equipped to explore a given area of research more intensively than in the case of a conference covering many phases of a major discipline.

Each conference should be designed to stimulate further thought and activity on the subject, but a secondary objective is the provision of a suitable outlet for completed investigations. The critical factor upon which the success of a scientific meeting depends seems to be related to an adequate opportunity for informal discussion, if one may judge from the after-hours "bull sessions" in which individuals having similar professional interests congregate and talk shop.

This natural inclination to informal discourse must be exploited. Informal colloquia may be extremely helpful when convened subsequent to, or in connection with, the formal presentation of papers. An uncrowded program of prepared papers (perhaps as few as five or six per day) permits sufficient time for a full discussion of each paper immediately after its presentation, when interest in comment and criticism is at its peak. In the discussions legitimate differences of opinion and serious attempts at poignant speculation should be encouraged.

Ordinarily it is difficult to assess the merits of a liberal policy of conference administration, because the benefits may not appear until months or years later, often disguised beyond recognition. Occasionally, however, the inspiration for a significant piece of research can be traced directly to a particular scientific meeting.

The reporting phase, too, should continue the objective of the conference—the encouragement of further research. Published abstracts of invited papers, short summaries of the meeting in scientific journals, and private communications all aid in the rapid dissemination of noteworthy items. In the case of a conference dealing intensively with a particular subject, however, a carefully edited report may have great value as a reference volume. It should be made available not only to the participants, but also to the large group of interested researchers who could not attend the meeting, and to the even larger number of junior scientists and students who may thereby be motivated to enter the field. The impromptu discussions are usually rich in new ideas and in promising suggestions for further study; hence these, as well as the formal papers, should be included in the report. The editing of conference proceedings should entail a check of all statements for accuracy and an integration of the discussion into a coherent and logically connected unit. Commonly, supplementary explanatory material must be included for the benefit of scientists who are not as highly specialized in the field under discussion as the participants at the conference. In this way a scientific conference, designed to inspire maximum creative effort, will possess lasting values for all workers specializing or interested in the subject considered.

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THE time of year is upon us when we in the sciences eagerly scan the advance programs of meetings to be held by our societies. With a red pencil, we check this paper and that as being of interest. We check the times when they are to be presented so that a smooth working schedule will result in a maximum number of papers being covered. Some of us may even be paying our own expenses to the meetings so that we may, in a short time, catch up with progress in our own and related fields.

Unfortunately, attendance at the meetings often dulls the edge of anticipation. Many of the papers thought to be of importance turn out to be "duds"—not because the work covered is of little importance, but simply because the persons giving them fail to observe a few simple but important details.

This communication is, therefore, addressed to colleagues who intend to present papers at future meetings. It not only applies to the neophyte but to veterans of many a meeting, for the beginner is sometimes more likely to be careful in his presentation than the veteran. The work you are reporting is important to you; otherwise you would not be presenting it. In nine out of ten cases, however, the listener would not suspect it. The manner in which a paper is given is as important as its content. You must convey the importance of the work to your listeners; if not, you are wasting your time and theirs, too.

Here are some criticisms usually heard about speakers at scientific meetings:

1. The speaker lacked enthusiasm. The listener thinks, "This fellow doesn't seem too interested in his work. He reads the paper as if it were the first time he had seen it. The slides are strange to him, too!" (More about slides later.)

2. The speaker drones on and on in a monotone. Talk with normal inflection as you would when describing a baseball game. Also talk about twice as loud as you normally do. After all, the room is large and crowded, and some of us can tune up our hearing aids just so far. Also, we may have to contend with the two gentlemen on our right who are still discussing the previous paper.

3. In describing his slides the speaker turns his back to the audience. The listeners' only hope of hearing him is that perhaps his words will be reflected as is the picture.

4. The speaker is afraid the listener will forget what organism or compound he is talking about, so every time a reference is made to it, the exact name is used. One recent speaker mentioned "*Micrococcus pyogenes* var. *aureus*" at least 25 times in a paper he was presenting.

He could have saved himself and his audience at least two minutes had he referred simply to "the organism."

5. Most speakers try to squeeze too much into one slide. The print is usually too small. Large freehand printing is at least readable, if not as neat as ordinary typewriting, which can't be read anyhow. Give your audience time to read your important data. One frequently hears a speaker allude to a slide when it comes on the screen, "This slide isn't too important." So flip! . . . we go on to the next. If it isn't too important, why include it? Almost every institution, whether it be educational, governmental, or industrial, has someone who is more or less expert on visual aids. It will pay to consult him before having slides prepared. Your slides, if they are readable and clear, will help tell your story more easily.

If speakers would keep these points in mind, our meetings would certainly be a greater success. Remember that some of your listeners may have come especially to hear your paper. How often one hears the remark, "The title sounded so good, but what a waste of time!"

PAUL F. KLENS

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University of Michigan Geological Field Work in Mexico

A PROGRAM of studies of sections across the Mexican geosyncline at right angles to the marginal land masses has been designed to determine lateral variations in structure, lithology, and faunal relationships of successive geologic formations. Although purely scientific, these regional studies have economic implications. Their bearing on ore deposition is threefold: (1) to provide the regional setting for detailed studies of structure in the mines and mining districts along the eastern edge of the Sierra Madre Occidental; (2) to place the age of the prelava sedimentary rocks on a sound regional and paleontologic basis; (3) to locate intrusive bodies with respect to mineralization. Petroleum exploration may be guided by the interpretation of geologic history resulting from the series of stratigraphic sections measured in mountain ranges of the Plateau Central. The sequence of faunas and faunal zones recognized in each formation provides useful markers, which should be found in wells penetrating the subsurface. Structural features mapped in the mountain ranges can be projected into the basins, where geologic conditions may be obscure.

Field work in northern Mexico in the area of the early Mesozoic "Coahuila Peninsula" was resumed during July and August 1952 by a party from the Museum of Paleontology of the University of Michigan. Lewis B. Kellum, in charge of the program, was accompanied by two graduate students, Bob F. Perkins, of Dallas, Tex., and Cecil C. Kersting, of Muskegon, Mich. The primary purpose of the investigation was to study the fauna of the Lower Cretaceous Aurora limestone and the geologic relationships of the Aurora limestone to the Cuchillo evaporites.

The area mapped is along the Durango-Coahuila state line in the central part of the Sierra de Tlahualilo, about 250 miles south of the international border at the Big Bend of the Rio Grande. The general structure of the Sierra de Tlahualilo in Cretaceous strata is a broad, northward-trending anticline. On this major structure is superimposed a variety of well-defined local deformations. A small area of volcanic rocks encroaches on the western side of the range.

Three stratigraphic sections were measured. Small patches of fossiliferous platy limestones and yellow marls of the Indidura formation were found beneath the volcanics resting on the Aurora limestone. Fossils were collected at four horizons in the Aurora, the lowest of which occurs in a silicified zone that may mark the top of the Cuchillo formation. The limestones below this zone weather darker gray, are interbedded with gypsum, and grade downward into the highly gypsiferous beds of the Cuchillo formation. Rudistids occur at the top of the Aurora limestone but are not the dominant element in the molluscan fauna. A faunal zone about 600 ft below the top is characterized by a large assemblage of pelecypods, gastropods, brachiopods, and echinoids, of which *Gryphaea marcoui* Hill is the most abundant form. This zone, present throughout the area mapped, proved to be a most reliable datum plane in a thick limestone section. A few feet above this zone nautiloid cephalopods were found at several localities. The faunas from the Aurora will be studied in the Museum of Paleontology during the coming year.

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A New Medium for Modeling Microscopic Structures in Three Dimensions

A FREQUENTLY annoying problem in research is the difficulty encountered in reconstructing a microscopical structure in a three-dimensional model large enough to allow effective study and yet not requiring too much time in preparation. This difficulty was experienced by the author while studying the embryonic development of the oriental fruit moth *Grapholitha molesta* Busck, the egg of which measures 0.7×0.4 mm. The embryo is coiled within the egg in such a fashion that the usual methods of orienting the block for sectioning yielded cross, longitudinal, and oblique sections of the same embryo, and an understanding of its orientation within the egg was important.

After blotting paper, cardboard, balsa, and wax sheets proved unsatisfactory, self-hardening sculptor's clay was found to be excellent for modeling, in that it reduced construction time, made greater detail possible, and resulted in a nearly indestructible product.

Modeling consists of three distinct steps: preparation of the clay, cutting the clay section, and building the model. A ball of clay of appropriate size is placed between two sheets of waxed paper. This sandwich is laid on a sheet of glass, rolling guides are put into place, and the ball is rolled into a slab of proper

thickness with a rolling pin. The thickness of the rolling guides depends upon the desired magnification; for example, if the specimen were sectioned at 8 μ and the desired magnification through a camera lucida system were 200×, the thickness of the clay slab representing each section would be $8 \times 200 = 1600$ μ, or 1.6 mm. Since clay slabs greater than 2 mm in thickness are more easily handled, it is better to double the thickness of the calculated slab and use alternate sections on the slide. When the clay slab has been rolled out, the top piece of waxed paper is stripped off, and the slab, still on the glass, is transferred to the camera lucida field.

The outline of the section image projected onto the clay through the camera lucida system is then traced with a scalpel or stout dissecting needle, with sufficient pressure to cut out the clay section from the slab. The clay section is then inverted on the glass plate, the second piece of waxed paper stripped off, and the clay that was not a part of the section removed. The clay section is carefully lifted from the glass and placed on the model. The next clay section is cut and placed on top of the first after the two interfaces have been wet with water. The remaining sections follow in like manner. After a number of sections have been pieced together, details are sculptured into the soft clay.

In the case of a round specimen in which the first section is too small to support the increasingly heavier sections placed upon it, construction must start somewhere in the middle, preferably with the largest single section, and be continued outward to the smallest. Care must be taken to build the second half in reverse so that the two halves can be joined. Compression of the lower sections by the weight of new sections can be prevented by allowing the lower sections partially to dry so that the harder clay will support additional weight. A partly completed model can be kept pliable for subsequent work if wrapped in damp toweling.

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Color in Trilobites

IN SCIENCE (**117**, 17 [1953]) appears M. W. Garretson's interesting note on "Color in Trilobites of Trenton Age." The author states "no mention of color in any trilobites has been found in the literature." Possibly this should read "Ordovician" rather than "any trilobites." In 1922 there appeared the following: "A Trilobite Retaining Color-Markings" (Raymond, P. E. *Am. J. Sci.*, **4**, 461). In this article Raymond described with a figure a pygidium of *Anomocare vittata*, which he collected from the Cambrian of Cherokee County, Alabama, in 1921, and which shows retention of color markings. I personally recall having seen this specimen while a student of Raymond's.

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β-Glucuronidase and Catalysis

IN a recent exchange of comments with Levvy (SCIENCE, **116**, 285 [1952]), Fishman reiterated his view that the enzyme β-glucuronidase catalyzes the biosynthesis of conjugated glucuronides. Certain aspects of this question merit further comment. The Fishman hypothesis is representative of a waning genre which perhaps culminated with Bergman's espousal of the peptidases as the agents directly responsible for protein synthesis. Before the role of adenosine triphosphate (ATP) in the transfer of energy was appreciated, it was not possible to discover the rather complex experimental conditions necessary to demonstrate biological syntheses with crude tissue preparations. On the other hand, much information was available on amidases, esterases, and glycosidases, and it was a fashionable presumption, still encountered occasionally in other instances than the case under discussion, that these hydrolytic enzymes, because of some vague, unknown, and rather mysterious special environmental situation within the cell, caused a synthesis of the compounds which in prosaic *in vitro* experiments were cleaved rather than created. This presumption had a special advantage for its advocates in that, by asserting the necessity for a duplication of an unknown condition existing intracellularly if synthesis was to be demonstrated, it became impossible to bring direct experiments to bear on the problem, and the presence of a hydrolytic enzyme in a tissue could be invoked to argue either for the synthesis or the hydrolysis of a given substrate, depending upon which side the investigator desired to lean toward. One can agree with Fishman that these questions, along with adherence to the atomic theory, are matters of personal opinion, but not that his hypothesis is innocuous, even if fallacious. As an example, anyone who utilizes changes in tissue glucuronidase activity under varying experimental conditions as an index of changes in the ability to conjugate steroids is wasting his time if the Fishman hypothesis is wrong.

In addition to the convincing objections advanced by Levvy, attention should be drawn to the necessity of differing routes of synthesis and hydrolysis if the cell is to exist in a dynamic state. At a given moment a single enzyme cannot be catalyzing a net reaction in opposite directions. Further, a hydrolytic process, even if thermodynamically reversible at reasonable concentrations, is at the mercy of changing levels of intracellular constituents. This is perhaps why cells have evolved mechanisms of synthesis linked to highly exergonic reactions, thus enabling the processes of metabolism to continue at low substrate levels. It should be remembered that all cells employ the uronic acids as structural components, and the formation of these more important glycosides, in addition to the rather special hormone conjugates with which Fishman has been concerned, must also be accounted for.

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Book Reviews

Quantitative Chemical Analysis. 10th ed. Leicester F. Hamilton and Stephen G. Simpson New York: Macmillan, 1952. 529 pp. Illus. $4.50.

This book is the tenth edition of one first published in 1897 by H. P. Talbot. Any such work must have real merit to survive for half a century.

The chief question is what changes have been made in the latest edition. Although numerous, in general these represent efforts to clarify the presentation and to modernize the material. Thus, theory is expanded and some newer methods are substituted for older ones. For individual methods the general form is the statement of principles and theory, the detailed operating directions, and the representative numerical problems.

The over-all emphasis remains on titrimetric and gravimetric methods, in that order. Altogether, this treatment seems conservative and sound.

Some of the definitions used do not agree with the recent recommendations of the nomenclature committee of the Division of Analytical Chemistry of the American Chemical Society; e.g., the first sentence on page 285 "ain't necessarily so," for the sample may not be weighed or dissolved, or the desired constituent separated from solution. The outline on page 393 is not sufficiently inclusive to cover a number of different kinds of methods.

The reviewer retains the generally high opinion of this book which he has held for recent editions.

Quantitative Chemical Analysis: An Introduction to the Science and Practice of Chemical Measurement. Charles W. Foulk, Harvey V. Moyer, and William M. MacNevin. New York–London: McGraw-Hill, 1952. 484 pp. $5.00.

Although this book is printed as a first edition, it brings back to the reviewer many recollections of the senior author's much earlier work. As an example, separate discussion of theory and practice is retained in the new work. Incidentally, the reviewer now accepts the soundness of this viewpoint. He cannot agree, however, with the general implications of the proposed classification of analytical methods. Nor does he believe that the process of precipitation has any essential connection with gravimetry. The former is a means of separation, the latter a kind of measurement.

The theoretical part (280 pp.) deals primarily with gravimetry (including precipitation) and titrimetry. Included also are short chapters on errors, oxidation-reduction potentials, potentiometric determination of pH, electrometric titrations, electrodeposition, and colorimetric analysis.

Most of the laboratory exercises are gravimetric or titrimetric, thus following the general pattern still popular in many institutions. The number and variety seem adequate, although admittedly no two instructors would agree on what to include in such a list. Useful items are included in the appendix.

In one form or another, much of the material in this book has been used with large classes for two to four decades. It is thus a work of proved value. In the new, expanded form, it should interest many teachers.

M. G. MELLON

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Allgemeine Physiologie. Albrecht Bethe. West Berlin: Springer-Verlag, 1952. 294 pp. Illus. DM 29.70.

The author of this book is the dean of the German physiologists. In his ripe old age—he celebrated his 80th birthday a few months ago—he presents a small but rich general physiology. The subject matter of this area of the biological sciences is less well defined than that of other parts of physiology. The influence of Verworn, who tried to base a general physiology largely on the study of unicellular organisms, can be traced in Bethe's book. Other aspects, however, such as the physicochemical organization of the protoplasms, are duly emphasized—particularly permeability, vital staining, and ion effects. The relation of stimulus to excitation, bioelectricity, the general physiology of movements, the principles of nervous conduction, and of the action of hormones are also dealt with.

This is one of those rare books which the expert enjoys and which ought to be profitable for the beginner. It is well written, not overloaded with facts, and is rich in ideas. It would be highly desirable if medical students and students of mammalian physiology would first become acquainted with general physiology as discussed here before they approach the intricacies of human physiology.

Printing and binding of the book are excellent.

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Scientific Book Register

Filter Design Data for Communication Engineers. J. H. Mole. New York: Wiley, 1952. 252 pp. Illus. $7.50.

Iodine Content of Foods. Annotated bibliography 1825–1951 with review and tables. London: Chilean Iodine Educational Bureau, 1952. (Distributed by Lange, Maxwell & Springer, London.) 183 pp. 21s.

Linear Algebra and Projective Geometry. Vol. II of Pure and Applied Mathematics: A Series of Monographs and Textbooks; Paul A. Smith and Samuel Eilenberg, Eds. Reinhold Baer. New York: Academic Press, 1952. 318 pp. Illus. $6.50.

Theory of Electric Polarisation. C. J. F. Böttcher. Amsterdam–Houston: Elsevier, 1952. 492 pp. Illus. $10.00.

Respiration in Plants. 3rd ed. Walter Stiles and William Leach. London: Methuen; New York: Wiley, 1952. 172 pp. Illus. $2.25.

Soluble Silicates: Their Properties and Uses. Vol. 1, *Chemistry.* James G. Vail, with assistance of John H. Wills. New York: Reinhold, 1952. 357 pp. Illus. $9.00.

Mechanics: Lectures on Theoretical Physics, Vol. I. Arnold Sommerfeld; trans. from 4th German ed. by Martin O. Stern. New York: Academic Press, 1952. 289 pp. Illus. $6.50.

Encyclopédie Biogéographique et Écologique. Vol. VIII, *Faune des Nids et des Terriers en Basse Côte d'Ivoire.* C. Delamare Deboutteville and R. Paulian. Paris: Paul Lechevalier, 1952. 116 pp. 1350 fr.

Textbook of Engineering Materials. Melvin Nord. New York: Wiley; London: Chapman & Hall, 1952. 518 pp. Illus. $6.50.

A General Zoology of the Invertebrates. 3rd ed. G. S. Carter. London: Sidgwick & Jackson; New York: Macmillan, 1948–52. 509 pp. Illus. $5.75.

The Methods of Statistics. 4th ed. L. H. C. Tippett. New York: Wiley; London: Williams & Norgate, 1952. 395 pp. Illus. $6.00.

Field Geology. 5th ed. Frederic H. Lahee. New York–London: McGraw-Hill, 1952. 883 pp. Illus. $8.50.

Associated Measurements. M. H. Quenouille. New York: Academic Press; London: Butterworths, 1952. 242 pp. Illus. $5.80.

Association Affairs

Constitution and Bylaws

Howard A. Meyerhoff, *Administrative Secretary*

At its first session at St. Louis on Dec. 27, 1952, the AAAS Council passed the revised Constitution and new Bylaws without a dissenting vote. Although both documents were published in SCIENCE (**116**, 575 [1952]), the Constitution stipulates that they be reprinted in both Association journals and also that they become effective one month from the date on which Council action was taken—Jan. 27, 1953. Hereafter, and until amended, the work of the Association and its officers will be governed by the Constitution and Bylaws as printed below:

Constitution

Article I

Section 1. The American Association for the Advancement of Science was incorporated by an act of the General Court of the Commonwealth of Massachusetts in 1874. The Association is a nonprofit scientific and educational body.

Section 2. The objects of the American Association for the Advancement of Science are to further the work of scientists, to facilitate cooperation among them, to improve the effectiveness of science in the promotion of human welfare, and to increase public understanding and appreciation of the importance and promise of the methods of science in human progress.

Article II

Section 1. The membership of the Association shall consist of Members, Fellows, and Associates. Individuals in any of these three groups may become life members, emeritus members, and sustaining members in accordance with the provisions of Section 5 of this Article and with such relevant rules as the Board of Directors shall have prescribed.

Section 2. Members. Any person, institution, or organization may be admitted to the grade of Member. Each Member shall have such rights and privileges and shall pay such annual dues and fees as the Council shall have prescribed.

Section 3. Fellows. Any person who shall have made a meritorious contribution to science may become a Fellow of the Association under such procedures as the Board of Directors shall have prescribed.

Section 4. Associates. Any person who shall have a record of leadership in any field related to science and who wishes to cooperate in the advancement of science may become an Associate of the Association under such procedures as the Board of Directors shall have prescribed.

Section 5. (*a*) *Life Members.* Any person making the Association a life-membership contribution of such amount as the Board of Directors shall have prescribed may be admitted to life membership. Each Life Member shall be exempt from the payment of annual dues and shall have all the privileges of an annual member throughout life.

(*b*) *Emeritus Members.* Any individual annual member may be admitted to emeritus membership under such conditions as the Board of Directors shall have prescribed. Each Emeritus Member shall be exempt from the payment of annual dues and shall have all the privileges of an annual member throughout life.

(*c*) *Sustaining Members.* Any person making to the Trust Funds of the Association a sustaining membership contribution of such amount as the Board of Directors shall have prescribed shall be the founder of a Sustaining Membership, which shall bear his name and shall be maintained in perpetuity as a trust. Each incumbent of a sustaining membership shall have all the privileges of a life member. The first incumbent of a sustaining membership may be either the founder himself or another person named by him, as he may choose. On the death or resignation of an incumbent, the Board of Directors shall name another person to hold the membership throughout life.

Article III

Section 1. The officers of the Association shall be (*a*) general officers elected from among the Fellows by ballot of the Council, and (*b*) administrative officers elected by the Board of Directors as prescribed in Section 3 of this Article.

Section 2. General Officers. The general officers of the Association shall be a president-elect, a president, a retiring president, and a vice president for each section. The term of office of the president-elect and of the vice presidents shall begin on the January 15 following their

election. At the close of the one-year term of the president-elect he shall become president, and at the close of the one-year term of the president he shall become retiring president. In the event of a vacancy in the office of the president, the president-elect shall become president. In the event of a vacancy in the office of president-elect, the Board of Directors shall make a pro tempore appointment to hold until the vacancy shall have been filled by ballot of the Council. In the event of a vacancy in the office of vice president the Board of Directors shall fill the vacancy by appointment.

Section 3. Administrative Officers. The administrative officers shall be an administrative secretary, one or more associate or assistant secretaries, a treasurer, and, in addition, a secretary for each section. The administrative secretary, the associate or assistant secretaries, and the treasurer shall be elected by the Board of Directors. The secretaries of the sections shall be nominated from among the Fellows by the respective section committees and elected by the Board of Directors. The terms of office of each administrative officer shall be determined by the Board of Directors. The Board of Directors shall fill vacancies in the administrative offices.

Section 4. The duties of the officers shall be customary to those of the office and as further defined in the bylaws.

Article IV

Section 1. The Council shall perform duties prescribed in the constitution and shall act as an advisory body in matters pertaining to the general policies of the Association.

Section 2. The Council shall consist of (*a*) the president-elect, the president, the retiring president, the vice presidents, the secretaries of the sections, the administrative secretary, the treasurer, and the eight (8) elected members of the Board of Directors; (*b*) one Fellow elected by each regional division of the Association; and (*c*) the representatives of affiliated organizations as provided in Article VIII of this constitution. Each Council member shall serve until his successor shall have taken office. The president shall be chairman of the Council; if the president shall be unable to serve as chairman at any session, the Council members in attendance shall elect a chairman for that session. Twenty (20) members of the Council shall constitute a quorum for the transaction of business.

Section 3. The Council shall meet during the annual meeting of the Association and at other times on the call of the president or upon the written request of twenty (20) members of the Council.

Article V

Section 1. The Board of Directors is the legal representative of the Association and as such shall have, hold, and administer all the property, funds, and affairs of the Association.

Section 2. The Board of Directors shall consist of eleven (11) members, the president-elect, the president, the retiring president, and eight (8) Fellows elected by the Council, two each year, for a term of four years. At any election of members of the Board of Directors not more than one Fellow serving his fourth consecutive year as an elected member may be re-elected. In the event of a vacancy in the office of an elected member of the Board of Directors, his successor for the remainder of the year shall be elected from among the Fellows by the Board of Directors and, for the remainder of the unexpired term, his successor shall be elected by the Council at the next annual election. Five (5) members of the Board of Directors shall constitute a quorum for the transaction of business. The retiring president of the Association shall be chairman of the Board of Directors. If he shall be unable to serve at any session of the Board, the Board members in attendance shall elect a chairman for that session. The administrative secretary and treasurer shall be ex officio members of the Board of Directors without vote.

Section 3. The Board of Directors shall hold four (4) meetings a year, one of which will be at the annual meeting. The Board of Directors shall also meet at the call of the chairman.

Section 4. The Board of Directors shall appoint such committees as may be necessary to aid in the management of the Association. The duties of standing committees shall be stated in the bylaws.

Section 5. The term of office of each of the eight (8) regularly elected members of the Board of Directors shall begin on January 15 following his election, and each shall serve until his successor shall have taken office.

Article VI

Section 1. The Association shall be organized in sections in accordance with the fields of interest of its members, as determined by the Council. Each member of the Association may designate the section in which he wishes to be enrolled and may designate an additional section in which he is interested.

Section 2. The vice president for a section shall be ex officio chairman of that section.

Section 3. The affairs of each section shall be managed by a section committee consisting of (*a*) the chairman and secretary of the section; (*b*) other members of the Council whose professional interests are in the field covered by the section or who represent societies affiliated with the section; and (*c*) four (4) Fellows, one elected each year by the section committee for a term of four (4) years. No person shall serve concurrently in more than one section committee. If an elected member of a section committee shall have resigned or died, his successor for the remainder of the unexpired term shall be elected from among the Fellows by the Board of Directors from nominations made by the section committee. One third of the members of the section committee shall constitute a quorum for the transaction of business.

Section 4. The section committee of each section shall promote the work of the Association in its own field and may organize subcommittees for that purpose. It shall arrange such section programs as it shall deem desirable for meetings of the Association, either separately or in cooperation with other sections of the Association or with independent societies. With the approval of the Board of Directors a section committee may arrange section meetings to be held at places and times other than those of Association meetings.

Article VII

Section 1. Regional divisions and local branches of the Association may be authorized by vote of the Council, for the purpose of promoting the work of the Association in their respective territories.

Section 2. Each regional division or local branch shall elect its officers for such terms as it shall prescribe and shall hold its meetings and conduct its affairs as it shall deem desirable, subject to the relevant provisions of this constitution and of the bylaws of the Association, and to such special provisions as the Board of Directors of the Association shall have established.

Article VIII

Section 1. To facilitate cooperation between the Association and other organizations, and among the latter, the Council may, on recommendation of the Board of Directors, elect an organization to be an official affiliate.

Section 2. Each organization thus designated an affiliate shall be entitled to name one Fellow of the Association to represent it on the Council; if it has more than 100 members who are Fellows of the Association, it shall be entitled to name an additional Fellow to represent it on the Council.

Section 3. On recommendation of the Board of Directors, the Council may elect an organization to be an official associate. Associated organizations shall have the same rights and privileges as affiliated organizations except for representation on the Council.

Article IX

Section 1. The Association shall hold an annual meeting at such time and place each year as the Board of Directors shall have determined. Other meetings of the Association or of its sections may be authorized by the Board of Directors.

Article X

Section 1. The publications of the Association shall be issued in such manner as the Board of Directors may direct.

Article XI

Section 1. Funds of the Association shall be classified as Current Funds, Investment Funds, and Trust Funds.

(*a*) *Current Funds* shall include all dues of annual members, all receipts from publications, and all other funds received in the continuing operations of the Association.

(*b*) *Investment Funds* shall include all gifts and bequests received without special restriction concerning the use to be made of principal and income, and such other funds as may be designated by the Board of Directors as investment funds.

(*c*) *Trust Funds* shall consist of all life-membership contributions, all sustaining-membership contributions, all funds appropriated by the Board of Directors for establishing special life memberships, all gifts and bequests accepted with specific restrictions prohibiting their allotment to either Current Funds or Investment Funds, and such other funds as may be designated by the Board of Directors as Trust Funds.

Section 2. The deposit, investment, and disbursement of all funds shall be subject to the direction of the Board of Directors.

Article XII

Section 1. Amendments to this constitution shall be approved by the Board of Directors after publication in substance in SCIENCE and THE SCIENTIFIC MONTHLY at least one month prior to an annual meeting of the Association and ratified by a two-thirds vote of the Council members present in a Council session of that meeting. Ratified amendments shall be effective upon adoption and shall be published promptly in SCIENCE and THE SCIENTIFIC MONTHLY.

Bylaws

Article I

Section 1. The objects of the Association shall be accomplished by conducting meetings and conferences of those interested in various branches of science and education, producing and distributing publications, administering gifts and bequests as prescribed by the donors thereof, supporting research, making awards to recognize accomplishments in science, cooperating with other organizations in the advancement of science, and engaging in such other activities as shall have been authorized by the Board of Directors.

Article II

Section 1. Members who have paid dues for fifty years may be excused from further payments and still retain all the privileges of membership.

Section 2. Members may be elected by the Board of Directors to be Fellows of the Association and Fellows so elected shall remain Fellows only so long as they retain membership. If a Fellow discontinues his membership and subsequently rejoins the Association, he shall automatically again become a Fellow from the time of rejoining, without another election. Members are eligible to nomination for fellowship if they have contributed to the advancement of science either by the publication of original research or in other significant manner. Nominations for election to fellowship may be made by any three Fellows or by the administrative secretary or by the section committee in whose field the nominee's scientific work mainly lies.

Section 3. A Member may be dropped from membership for conduct which in any way tends to injure the Association or to affect adversely its reputation or which is contrary to, or destructive of, its objects. Charges of injurious conduct shall not be entertained against a Member unless the precise nature of the charges be submitted in writing to the president of the Association by not fewer than two Members. Upon receipt of such charges, the president shall refer them to the Executive Committee, which shall have the power to determine whether the charges shall be dropped, whether the accused shall be given an opportunity to resign, or whether the charges shall be referred to the Board of Directors for review and for final disposition. Whenever charges are referred to the Board of Directors, no person shall be dropped from membership except after opportunity to be heard and then only by a three-fourths vote of those members of the Board of Directors present and voting at a regular or special meeting.

Article III

Section 1. The administrative secretary shall serve as secretary to the Council and to the Board of Directors; he shall be in charge of the Association's offices and shall manage the affairs of the Association in accordance with procedures determined by the Board of Directors. He shall be an ex officio member of all standing committees.

Section 2. The treasurer shall perform the usual duties and those assigned in the bylaws.

Section 3. Reports of the administrative secretary and the treasurer shall be made in the manner prescribed by the Board of Directors.

Article IV

Section 1. The committees shall be standing as provided in the bylaws or special as the Board of Directors approves.

Section 2. During the interim between meetings of the Board of Directors, an Executive Committee consisting of the retiring president, the president, the president-elect, and such other directors or administrative officers as the Board of Directors may designate shall act on behalf of the Board of Directors. All actions taken by the Executive Committee shall be submitted for review

and action at the next following meeting of the Board of Directors.

Section 3. The Investment and Finance Committee shall advise the Board of Directors regarding purchases and sales of securities for the Association, shall make recommendations to the Board of Directors on financial questions, and shall have the authority to buy or sell securities under such limitations as the Board of Directors may set. The Investment and Finance Committee shall consist of the treasurer, the administrative secretary, and five (5) members appointed by the Board of Directors. Each appointed member shall serve a term of five (5) years, the term of one member expiring on January 14 of each year. Each shall serve until his successor shall have taken office.

Section 4. The Committee on Affiliation and Association shall review applications for affiliation or association with the Association and make recommendations thereon to the Board of Directors. The committee shall consist of five (5) members appointed by the Board of Directors. Each member shall serve a term of five (5) years, the term of one member to expire on January 14 of each year. Each shall serve until his successor shall have taken office.

Section 5. The Publications Committee shall give continuing scrutiny to the publications of the Association and the policies pertaining thereto and shall make recommendations thereon to the Board of Directors. The committee shall consist of five (5) men appointed by the Board of Directors. Each member shall serve a term of five (5) years, the term of one member to expire on January 14 of each year. Each shall serve until his successor shall have taken office.

Article V

Section 1. Council representatives of affiliated organizations which are not specifically related to an established section of the Association may be assigned to section committees in accordance with their requests.

Article VI

Section 1. Regional divisions authorized by the Council have full control of their meetings, of their affiliations with other scientific organizations, and of all activities to promote the advancement of science in their territory.

Section 2. The Pacific Division (organized in 1915) includes members of the Association resident in British Columbia, Washington, Oregon, California, Idaho, Nevada, Utah, and the Hawaiian Islands.

Section 3. The Southwestern Division (organized in 1920) includes members of the Association resident in Arizona, New Mexico, Colorado, Sonora, Chihuahua, and Texas west of the 100th meridian.

Section 4. The Alaska Division (organized in 1951) includes members of the Association resident in Alaska.

Section 5. Each division shall receive for its expenses an annual allowance not to exceed one dollar for each of its members in good standing and shall make an annual report to the Board of Directors covering its financial situation and other activities.

Article VII

Section 1. The names of affiliated and associated organizations shall be published from time to time as directed by the Board of Directors.

Section 2. Affiliated academies of science shall receive for research an annual allowance of fifty cents for each of their members who is also a member in good standing of the Association. The minimum annual allowance shall be fifty dollars. If any academy fails to utilize the research funds made available to it in any one year, these funds shall revert to the Association's treasury on December 31 of the second calendar year following the year in which the allowance was computed.

Article VIII

Section 1. The programs and arrangements for the Association meetings shall be under the general direction of the Board of Directors.

Article IX

Section 1. The publications of the Association shall be (*a*) SCIENCE, (*b*) THE SCIENTIFIC MONTHLY, (*c*) *Proceedings*, and (*d*) such other special publications as the Board of Directors may direct.

Section 2. The Association shall not be responsible for statements or opinions advanced in papers or in discussions at meetings of the Association or its sections, divisions, or branches, or printed in its publications.

Section 3. The Association reserves the right to copyright, at the discretion of the Board of Directors, any of its papers, discussions, reports, or publications.

Article X

Section 1. All funds shall be paid into the business office of the administrative secretary, where they shall be entered in the books of the Association, and deposited in a bank designated by the Board of Directors. The treasurer shall be the custodian of all Investment Funds, Trust Funds, and such other funds as may be placed in his charge by the Board of Directors. The administrative secretary shall be the custodian of the current funds.

Section 2. All bills against members and others shall be made and collected by the business office of the administrative secretary.

Section 3. All expenditures shall be made in accordance with the budget of appropriations as adopted by the Board of Directors.

Section 4. All payments shall be made by the business office upon competent certification as to their correctness and proper authorization.

Section 5. Checks against the accounts of the Association will bear two signatures, from a list of individuals determined by the Board of Directors.

Section 6. The securities of the Association may be bought, sold, or exchanged only upon the written order of two of the following: the chairman of the Investment and Finance Committee, the vice-chairman of the Investment and Finance Committee, the treasurer, and the administrative secretary.

Section 7. The business office of the administrative secretary shall keep proper accounts of all financial transactions of the Association.

Section 8. The accounts of the Association shall be audited and approved annually by a certified public accountant selected by the Board of Directors.

Section 9. The administrative secretary shall have the authority to enter into contracts for the Association, but contract authorizations must be within the budget authorizations made by the Board of Directors.

Section 10. The activities of the Gordon Research Conference shall be administered according to procedures established by the Board of Directors.

Article XI

The bylaws may be amended by majority vote of the Board of Directors, provided notification of the proposed amendment has been mailed to each member of the Board at least twenty (20) days prior to the meeting. Changes made in the bylaws by the Board of Directors shall be subject to approval, by majority vote, of the Council.

Publications Received

Birds of Washington Park, Albany, New York. Dayton Stoner and Lillian C. Stoner. New York State Museum, Bull. No. 344. Albany: University of the State of New York, Sept. 1952. 268 pp. Illus.

Blood-Brothers. An ethno-sociological study of the institutions of blood-brotherhood with special reference to Africa. Harry Tegnæus; trans. from the Swedish by Reginald Stedman and Donald Burton. New York: Philosophical Library, 1952. 181 pp. Illus. $12.00.

A Brief History of the Art of Navigation. An outline and background of the methods employed by navigators for finding their way around the seas. Louis Allen Hardin. New York: William-Frederick Press, 1952. 142 pp. Illus. $3.75.

Bulletin Climatologique Annuel du Congo Belge et du Ruanda-Urundi. Année 1951. Bureau Climatologique, Com. No. 5. Bruxelles: INEAC, 1952. 99 pp. 100 fr.

California Cooperative Sardine Research Program. Progr. Rept., Jan. 1, 1951–June 30, 1952. Sacramento: Calif. Dept. Fish and Game, Marine Research Committee, July 1, 1952. 51 pp. Illus.

Commonwealth Scientific and Industrial Research Organization, Fourth Annual Report for Year Ending Jun. 30, 1952. Melbourne: Commonwealth of Australia, 1952. 350 pp. Mimeo.

Fire Resistance of Concrete Floors. Daniel S. Goalwin. Building Materials and Structures Rept. 134. Washington, D. C.: National Bureau of Standards, 1952. ii + 11 pp. Illus. 15¢.

Fish-Culture in Brackish-Water Ponds of Java. W. H. Schuster. Indo-Pacific Fisheries Council, Spec. Pubs. No. 1. G. L. Kesteven, Ed. Trans: of Indonesian edition, 1950. Madras, India: Diocesan Press, 1952. xii + 143 pp. Illus.

Hanna's Handbook of Agricultural Chemicals. Lester W. Hanna. Portland, Ore.: West Coast Print. and Binding Co., 1952. 209 + xvi pp. Illus. $3.25. (Distr. by author, R. 1, Box 210, Forest Grove, Ore.)

Manual of Upper Extremity Prosthetics. A publication of the Artificial Limbs Research Project, under the supervision of the Advisory Committee on Artificial Limbs, National Research Council, supported by contract with the Veterans Administration. By the staff of the Artificial Limbs Project, UCLA; R. Deane Aylesworth, Ed. Los Angeles, Calif.: Artificial Limbs Project, Dept. of Engin., Univ. Calif., 1952. 9 sections. Illus. $2.00.

Marx and Science. J. D. Bernal. New York: International Pubs., 1952. 48 pp. $1.00.

Memorial Center for Cancer and Allied Diseases. Annual Report, 1951–1952. New York: Memorial Center for Cancer and Allied Diseases, 1952. 157 pp. Illus.

The New Dictionary of American History. Michael Martin and Leonard Gelber. New York: Philosophical Library, 1952. 695 pp. $10.00.

Pavement-Marking Materials. Highway Research Board Bull. 57. National Research Council Pub. 239. Washington, D. C.: NRC, 1952. vi + 128 pp. Illus. $1.80.

Pièces Épigraphiques de Ḥeid Bin 'Aqîl la Nécropole de Timnaʿ (Ḥagr Kohlân). Bibliothèque du Muséon. Vol. 30. A. Jamme. Louvain: Publications Universitaires, 1952. 252 pp. 26 pl. 375 fr.

Meetings & Conferences

Feb. 4–6. Western Computer Conference. Hotel Statler, Los Angeles.

Feb. 5–7. Southwestern IRE Conference and Electronics Show (Annual). Plaza Hotel, San Antonio.

Feb. 8–10. Congress on Medical Education and Licensure (Annual). Palmer House, Chicago.

Feb. 12–13. Protestant Hospital Association. Palmer House, Chicago.

Feb. 12–13. Southern Weed Conference. Jung Hotel, New Orleans.

Feb. 14–15. Society for the Study of Social Problems, joint with the Society for the Psychological Study of Social Issues. New York University, New York.

Feb. 15–17. Canadian Ceramic Society. Royal York Hotel, Toronto.

Feb. 16–19. Technical Association of the Pulp and Paper Industry (Annual). Commodore Hotel, New York.

Feb. 16–21. Pakistan Science Conference (Annual). Lahore.

Feb. 18–20. National Cotton Council (Annual). General Oglethorpe Hotel, Savannah, Ga.

Feb. 24. Society for the Advancement of Criminology (Interim). Northwestern University Law School, Chicago.

Feb. 26–28. American Academy of Forensic Sciences (Annual). Drake Hotel, Chicago.

Feb. 27. Society of Illinois Bacteriologists. Furniture Club, Chicago.

Mar. 1–6. International Congress of Military Medicine and Pharmacy. Montevideo.

Mar. 2–6. American Society for Testing Materials. Hotel Statler, Detroit.

Mar. 6–8. North American Wildlife Conference. Washington, D. C.

Mar. 7. Symposium on Air Pollution and its Control. Wagner College, Grymes Hill, S. I., N. Y.

Mar. 8–11. American Institute of Chemical Engineers. Buena Vista Hotel, Biloxi, Miss.

Mar. 11–13. National Agricultural Chemicals Association (Spring). Jung Hotel, New Orleans.

Mar. 11–Apr. 8. Commission for Synoptic Meteorology of the World Meteorological Organization. Washington, D. C.

Mar. 12–25. Commission for Climatology of the World Meteorological Organization. Washington, D. C.

Mar. 13–14. Alabama Academy of Science, Inc. Florence.

Mar. 16–18. Ciba Foundation Symposium on Preservation of Normal Tissues for Transplantation. London.

Mar. 16–20. National Association of Corrosion Engineers (Annual). Hotel Sherman, Chicago.

Mar. 17–19. American Meteorological Society, Symposium on Numerical Prediction; Climatology; Long-Range Forecasting; Ice Island. Atlantic City.

Mar. 19–21. Optical Society of America (Spring). Hotel Statler, New York.

Mar. 23–26. American Association of Petroleum Geologists, Society of Economic Paleontologists and Mineralogists, and Society of Exploration Geophysicists (Joint Annual). Coliseum, Houston.

Mar. 23–26. Institute of Radio Engineers (Annual). Waldorf-Astoria Hotel and Grand Central Palace, New York.

Mar. 23–27. Western Metal Congress and Exposition. Pan-Pacific Auditorium, Los Angeles.

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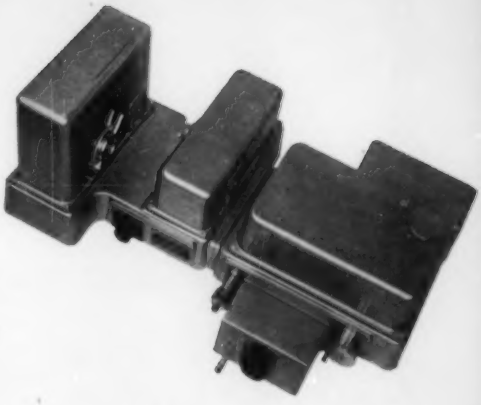

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